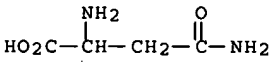
FILE 'REGISTRY' ENTERED AT 08:47:26 ON 24 JUL 2006

=> S ASPARAGINE/CN
L1 2 ASPARAGINE/CN

=> D 1-2

L1 ANSWER 1 OF 2 REGISTRY COPYRIGHT 2006 ACS on STN
RN 3130-87-8 REGISTRY
ED Entered STN: 16 Nov 1984
CN Asparagine (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Asparagine, DL- (8CI)
OTHER NAMES:
CN (±)-Asparagine
CN DL-Aspartamine
CN NSC 206243
CN NSC 7891
FS 3D CONCORD
MF C4 H8 N2 O3
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOSIS, CA, CAPLUS, CASREACT, CHEMCATS, CHEMLIST, CIN, CSCHEM, DETHERM*, GMELIN*, IFICDB, IFIPAT, IFIUDB, MSDS-OHS, PIRA, PROMT, SPECINFO, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**, NDSL**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)



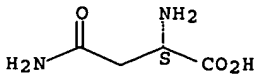
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

331 REFERENCES IN FILE CA (1907 TO DATE)
10 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
332 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L1 ANSWER 2 OF 2 REGISTRY COPYRIGHT 2006 ACS on STN
RN 70-47-3 REGISTRY
ED Entered STN: 16 Nov 1984
CN L-Asparagine (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Asparagine, L- (8CI)
OTHER NAMES:
CN (-)-Asparagine
CN (S)-2,4-Diamino-4-oxobutanoic acid
CN (S)-Asparagine
CN α-Aminosuccinamic acid
CN Agedoite
CN Altheine
CN Asn
CN Asparagine
CN Asparagine acid
CN Asparamide
CN Aspartamic acid
CN Aspartic acid β-amide
CN Aspartic acid amide
CN Butanoic acid, 2,4-diamino-4-oxo-, (S)-
CN Crystal VI
CN L-β-Asparagine
CN L-2,4-Diamino-4-oxobutanoic acid

CN l-Asparagine
CN L-Aspartamine
CN NSC 82391
FS STEREOSEARCH
DR 7006-34-0, 328-41-6, 32640-57-6
MF C4 H8 N2 O3
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, AQUIRE, BEILSTEIN*, BIOSIS,
    BIOTECHNO, CA, CABA, CAOLD, CAPLUS, CASREACT, CBNB, CHEMCATS,
    CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, DDFU, DETHERM*, DRUGU, EMBASE,
    GMELIN*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS,
    NAPRALERT, PIRA, PROMT, PS, RTECS*, SPECINFO, TOXCENTER, USAN, USPAT2,
    USPATFULL, VETU
      (*File contains numerically searchable property data)
    Other Sources: DSL**, EINECS**, TSCA**
      (**Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry.



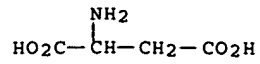
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

          16033 REFERENCES IN FILE CA (1907 TO DATE)
            514 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
          16058 REFERENCES IN FILE CAPLUS (1907 TO DATE)
              3 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

=> S ASPARTIC ACID/CN
L2   2 ASPARTIC ACID/CN

=> D 1-2

L2 ANSWER 1 OF 2 REGISTRY COPYRIGHT 2006 ACS on STN
RN 617-45-8 REGISTRY
ED Entered STN: 16 Nov 1984
CN Aspartic acid (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Aspartic acid, DL- (8CI)
CN DL-Aspartic acid
OTHER NAMES:
CN (±)-Aspartic acid
CN (RS)-Aspartic acid
CN Aminosuccinic acid
CN DL-Aminosuccinic acid
CN NSC 141379
FS 3D CONCORD
DR 874742-68-4
MF C4 H7 N O4
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOSIS, CA, CAPLUS,
    CASREACT, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, DETHERM*,
    GMELIN*, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MSDS-OHS, NAPRALERT, PIRA,
    PROMT, RTECS*, SPECINFO, SYNTHLINE, TOXCENTER, TULSA, USPAT2, USPATFULL
      (*File contains numerically searchable property data)
    Other Sources: DSL**, EINECS**, TSCA**
      (**Enter CHEMLIST File for up-to-date regulatory information)

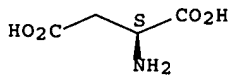


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1229 REFERENCES IN FILE CA (1907 TO DATE)
77 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1232 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L2 ANSWER 2 OF 2 REGISTRY COPYRIGHT 2006 ACS on STN
RN 56-84-8 REGISTRY
ED Entered STN: 16 Nov 1984
CN L-Aspartic acid (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Aspartic acid, L- (8CI)
OTHER NAMES:
CN (+)-Aspartic acid
CN (S)-Aminobutanedioic acid
CN (S)-Aspartic acid
CN 75: PN: WO2005016244 PAGE: 71 claimed protein
CN 7: PN: US20050014160 SEQID: 7 claimed protein
CN Asparagic acid
CN Asparaginic acid
CN Aspartic acid
CN Butanedioic acid, amino-, (S)-
CN H-Asp-OH
CN L-(+)-Aspartic acid
CN L-Aminosuccinic acid
CN L-Asparagic acid
CN L-Asparaginic acid
CN NSC 3973
CN NSC 79553
FS STEREOSEARCH
DR 6899-03-2, 181119-33-5
MF C4 H7 N O4
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, AQUIRE, BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CABA, CAOLD, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DETHERM*, DRUGU, EMBASE, GMELIN*, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NAPRALERT, PIRA, PROMT, PS, RTECS*, SPECINFO, SYNTHLINE, TOXCENTER, TULSA, ULIDAT, USAN, USPAT2, USPATFULL, VTB
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry. Rotation (+).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

40877 REFERENCES IN FILE CA (1907 TO DATE)
1333 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
40936 REFERENCES IN FILE CAPLUS (1907 TO DATE)
3 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

FILE 'CAPLUS' ENTERED AT 08:48:15 ON 24 JUL 2006

```
=> ACTIVATE ABZYME/Q
L3              QUE  ABB=ON  PLU=ON  ((CATALYSIS OR CATALYZES OR CATALYTIC OR C
                ATALYZED)(5A)ANTIBOD?) OR ABZYME

=> S L3
         183635 CATALYSIS
            424 CATALYSES
         183880 CATALYSIS
                  (CATALYSIS OR CATALYSES)
          36232 CATALYZES
         409364 CATALYTIC
             26 CATALYTICS
         409373 CATALYTIC
                  (CATALYTIC OR CATALYTICS)
         237243 CATALYZED
              1 CATALYZEDS
         237243 CATALYZED
                  (CATALYZED OR CATALYZEDS)
         466583 ANTIBOD?
           2370 (CATALYSIS OR CATALYZES OR CATALYTIC OR CATALYZED)(5A)ANTIBOD?
            262 ABZYME
            171 ABZYMES
            317 ABZYME
                  (ABZYME OR ABZYMES)
L4         2402 ((CATALYSIS OR CATALYZES OR CATALYTIC OR CATALYZED)(5A)ANTIBOD?)
                OR ABZYME

=> S ASPARAGINE
         30531 ASPARAGINE
           311 ASPARAGINES
L5       30649 ASPARAGINE
                  (ASPARAGINE OR ASPARAGINES)

=> S ASPARTIC ACID
         67749 ASPARTIC
       4180137 ACID
       1532069 ACIDS
       4672402 ACID
                  (ACID OR ACIDS)
L6       59566 ASPARTIC ACID
                  (ASPARTIC(W)ACID)

=> S L5,L1;S L6,L2
         16241 L1
L7       32919 (L5 OR L1)


         41782 L2
L8       67359 (L6 OR L2)

=> S L4(7A)(L7,L8)
L9           10 L4(7A)((L7 OR L8))

=> D 1-10 CBIB ABS

L9   ANSWER 1 OF 10  CAPLUS  COPYRIGHT 2006 ACS on STN
2005:346675   Document No. 142:392665  Preparation of amino acid derivatives as
     asparagine deaminase catalytic antibodies.
     Mulkerrin, Michael G.; Zhang, Ruoheng; Roskos, Lorin; Blumbergs, Peter;
     Lonescu, Dumitru (USA).  U.S. Pat. Appl. Publ. US 2005084488 A1 20050421,
     15 pp.  (English).  CODEN: USXXCO.  APPLICATION: US 2004-821626 20040409.
     PRIORITY: US 2003-462550P 20030410.
AB   Transition state analogs are described which may be used to elicit antibodies that
     catalyze the conversion of asparagine to aspartic acid. Synthetic schemes are disclosed
     for making the transition state analogs which can than be attached to a carrier mol. to
     form an immunoconjugate for administration to an animal for the purpose of raising
```

antibodies. Antibodies can in turn be used in pharmaceutical compns. which can be given to patients as part of a method of treating various conditions, particularly cancer. Examples describe the synthesis of 2-(acetylamino)-N-(1,4-dihydroxy-1-oxophospholan-3-yl)acetamide and N-glycyl-L-phosphonamidylalanine.

L9 ANSWER 2 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN

2003:20745 Document No. 138:200846 Molecular Dynamics Simulation Study of the Negative Correlation in Antibody AZ28-Catalyzed Oxy-Cope Rearrangement. Asada, Toshio; Gouda, Hiroaki; Kollman, Peter A. (Department of Pharmaceutical Chemistry, University of California, San Francisco, CA, 94143-0446, USA). Journal of the American Chemical Society, 124(42), 12535-12542 (English) 2002. CODEN: JACSAT. ISSN: 0002-7863. Publisher: American Chemical Society.

AB The oxy-Cope rearrangement reaction in the antibody AZ28 is investigated using ab initio MO calcns. and mol. mech. mol. dynamics simulations. This antibody, AZ28, is known as one of the few systems where the mature catalytic antibody shows a neg. correlation between the transition state analog (TSA) binding affinity and the catalytic rate of the oxy-Cope rearrangement compared to the germ line catalytic antibody. The ab initio optimized structure shows that the transition state structure has a more planar configuration than the TSA. The favorable electrostatic interactions between AZ28 and the transition state analog overcome the unfavorable van der Waals interactions; thus, AZ28 shows higher binding affinity for the TSA than the germ line. However, the AZ28 is not flexible enough to accept the relatively planar transition state structure. Because the lower flexibility causes poorer antibody-hapten interaction energies, the activation free energy of the oxy-Cope rearrangement becomes larger in the mature antibody than the germ line. We show that the differences in flexibility between the germ line and the mature form and the differences in structure between TSA and the transition state are the origin of the neg. correlation in AZ28-catalyzed oxy-Cope rearrangement. The mutation of residue 34 of the light chain, 34L, affects the binding free energies through the interresidue interaction because it is the closest to the hapten among the six mutatable residues. However, it does not affect the neg. correlation.

L9 ANSWER 3 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN

2000:336501 Document No. 133:146654 Catalytic antibodies for complex reactions: hapten design and the importance of screening for catalysis in the generation of catalytic antibodies for the NDA/CN reaction. DeSilva, Binodh S.; Orosz, Gyorgy; Egodage, Kamal L.; Carlson, Robert G.; Schowen, Richard L.; Wilson, George S. (Procter and Gamble Pharmaceuticals, Norwich, NY, USA). Applied Biochemistry and Biotechnology, 83(1-3), 195-208 (English) 2000. CODEN: ABIBDL. ISSN: 0273-2289. Publisher: Humana Press Inc..

AB Success in generating catalytic antibodies as enzyme mimics lies in the strategic design of the transition-state analog (TSA) for the reaction of interest, and careful development of screening processes for the selection of antibodies that are catalysts. Typically, the choice of TSA structure is straightforward, and the criterion for selection in screening is often binding of the TSA to the antibody in a microtiter-plate assay. This article emphasizes the problems of TSA design in complex reactions and the importance of selecting antibodies on the basis of catalysis as well as binding to the TSA. The target reaction is the derivatization of primary amines with naphthalene-2,3-dicarboxaldehyde (NDA) in the presence of cyanide ion. The desired outcome is selective catalysis of formation of the fluorescent derivative in preference to non-fluorescent side-products. In the study, TSA design was directed toward the reaction branch leading to the fluorescent product. Here, we describe a microtiter plate-based assay that is capable of detecting antibodies showing catalytic activity at an early stage. Of the antibodies selected, 36% showed no appreciable binding to any of the substrates tested, but did show catalytic activity in derivatizing one or more of the amino acids screened. In contrast, only two out of 77 clones that showed binding did not show catalysis. Thus, in this complex system, observation of binding is a good predictor of the presence of catalytic activity, and failure to observe binding is a poor predictor of the absence of catalytic activity.

L9 ANSWER 4 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN

1999:26468 Document No. 130:164688 Characterization and selectivity of

catalytic antibodies from human serum with RNase activity. Vlassov, Alexander; Florentz, Catherine; Helm, Mark; Naumov, Valerii; Buneva, Valentina; Nevinsky, Georgy; Giege, Richard (Institut de Biologie Moldculaire et Cellulaire, UPR 9002 du CNRS, Strasbourg, 67084, Germany). Nucleic Acids Research, 26(23), 5243-5250 (English) 1998. CODEN: NARHAD. ISSN: 0305-1048. Publisher: Oxford University Press.

AB IgG purified from sera of several patients with systemic lupus erythematosus and hepatitis B are shown to present RNA hydrolyzing activities that are different from the weak RNase A-type activities found in the sera of healthy donors. Further investigation brings evidence for two intrinsic activities, one observed in low salt conditions and another specifically stimulated by Mg2+ ions and distinguishable from human sera RNases. Cleavage of RNA substrates by the latter activity is not sequence-specific but sensitive to both subtle conformational and/or drastic folding changes, as evidenced by comparative anal. of couples of structurally well-studied RNA substrates. These include yeast tRNAAsp and its in vitro transcript and human mitochondrial tRNALys-derived in vitro transcripts. The discovery of catalytic antibodies with RNase activities is a first step towards creation of a new generation of tools for the investigation of RNA structure.

L9 ANSWER 5 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN

1998:309067 Document No. 129:78488 Evolving catalytic antibodies in a phage-displayed combinatorial library. Fujii, Ikuo; Fukuyama, Shiro; Iwabuchi, Yoshiharu; Tanimura, Ryuji (Biomol. Eng. Res. Inst, Suita, Osaka, 565, Japan). Nature Biotechnology, 16(5), 463-467 (English) 1998. CODEN: NABIF9. ISSN: 1087-0156. Publisher: Nature America.

AB In vitro affinity maturation for evolving catalytic antibodies has been demonstrated by generating a diverse repertoire of the appropriate complementarity-determining regions on a phage surface. Phage display is followed by a selection based on binding to an altered antigen that was not used at the time of immunization, and provides variants with new catalytic activity and substrate specificity. This library format reduces the time needed to isolate the desired catalytic antibody fragments to under 2 wk.

L9 ANSWER 6 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN

1998:196481 Document No. 129:13896 An antibody exo Diels-Alderase inhibitor complex at 1.95 Angstrom resolution. Heine, Andreas; Stura, Enrico A.; Yli-Kauhaluoma, Jari T.; Gao, Changshou; Deng, Qiaolin; Beno, Brett R.; Houk, Kendall N.; Janda, Kim D.; Wilson, Ian A. (Departments Molecular Biology and Chem., Skaggs Inst. Chem. Biol., La Jolla, CA, 10550, USA). Science (Washington, D. C.), 279(5358), 1934-1940 (English) 1998. CODEN: SCIEAS. ISSN: 0036-8075. Publisher: American Association for the Advancement of Science.

AB A highly specific Diels-Alder protein catalyst was made by manipulating the antibody repertoire of the immune system. The catalytic antibody 13G5 catalyzes a disfavored exo Diels-Alder transformation in a reaction for which there is no natural enzyme counterpart and that yields a single regioisomer in high enantiomeric excess. The crystal structure of the antibody Fab in complex with a ferrocenyl inhibitor containing the essential haptenic core that elicited 13G5 was determined at 1.95 angstrom resolution Three key antibody residues appear to be responsible for the observed catalysis and product control. Tyrosine-L36 acts as Lewis acid activating the dienophile for nucleophilic attack, and asparagine-L91 and aspartic acid-H50 form hydrogen bonds to the carboxylate side chain that substitutes for the carbamate diene substrate. This hydrogen-bonding scheme leads to rate acceleration and also pronounced stereoselectivity. Docking expts. with the four possible ortho transition states of the reaction explain the specific exo effect and suggest that the (3R,4R)-exo stereoisomer is the preferred product.

L9 ANSWER 7 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN

1993:404012 Document No. 119:4012 Engineering metal coordination sites into the antibody light chain. Wade, Warren S.; Koh, Jong S.; Han, Nianhe; Hoekstra, Denise M.; Lerner, Richard A. (Dep. Chem. Mol. Biol., Scripps Res. Inst., La Jolla, CA, 92037, USA). Journal of the American Chemical Society, 115(11), 4449-56 (English) 1993. CODEN: JACSAT. ISSN: 0002-7863.

AB A three-histidine Zn2+ binding site based on the carbonic anhydrase B site has been engineered into the four available sites on the light chain of the fluorescein binding antibody 4-4-20. All mutant antibodies bind fluorescein. Transition metal binding was assayed by tryptophan fluorescence quenching. Two of the four sites exhibit metal affinities consistent with complexation by three ligands. The specificity of the highest affinity site was probed by mutagenesis. For various combinations of histidine, aspartate, and glutamate residues, affinities range from -5 to -10 kcal/mol for Cu2+, -3 to -6.5 kcal/mol for Zn2+, and -3 and -5.5 kcal/mol for Cd2+. Binding is also observed between at least one mutant and Co2+ or Ni2+. The second highest affinity site shows a metal-dependent increase in fluorescein binding, indicating a ternary complex. Several ligand combinations give affinities in a potentially useful range for antibody catalysis with only four amino acid changes.

L9 ANSWER 8 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN

1991:469820 Document No. 115:69820 Antigens and abzymes for enhancing the rate of modification of metastable bonds. Powell, Michael J.; Rees, Anthony R.; Booth, Paul M.; Hong, Wonpyo; Titmas, Richard; Massey, Richard (IGEN Inc., USA). PCT Int. Appl. WO 9015074 A1 19901213, 46 pp. DESIGNATED STATES: W: AU, JP; RW: AT, BE, CH, DE, DK, ES, FR, GB, IT, LU, NL, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1990-US3226 19900607. PRIORITY: US 1989-364077 19890608.

AB Antigens capable of eliciting antibodies which can enhance the rate of chemical reactions at metastable bonds are disclosed. In particular, the rate of cleavage or formation of metastable peptide bonds, such as Asn-X, Asp-X, Gln-X, Glu-X, Lys-X, and His-Y-X, where X and Y are any amino acid, is enhanced by antibodies elicited by said antigen. The antigens contain a hapten which mimics the substrate at or near the site of the metastable bond, particularly a hapten which is immunol. cross-reactive to an amino acid sequence. Methods for selection of the bonds and desired haptens are described. The abzymes are produced by standard hybridoma methods. Prophetic peptide analogs to be used in the manufacture of abzymes for the cleavage of human immunodeficiency virus 1 gp120, IgE, and tumor necrosis factor are presented.

L9 ANSWER 9 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN

1991:181208 Document No. 114:181208 A mutagenesis study of a catalytic antibody. Jackson, David Y.; Prudent, James R.; Baldwin, Enoch P.; Schultz, Peter G. (Dep. Chem., Univ. California, Berkeley, CA, 94720, USA). Proceedings of the National Academy of Sciences of the United States of America, 88(1), 58-62 (English) 1991. CODEN: PNASA6. ISSN: 0027-8424.

AB Seven site-specific mutations were inserted in the genes encoding the variable region of the heavy chain domain (VH) of the phosphocholine- binding antibody S107. S107 is a member of a family of well-characterized highly homologous antibodies that bind phosphorylcholine mono- and diesters. Two of these antibodies, MOPC-167 and T15, have previously been shown to catalyze the hydrolysis of 4-nitrophenyl N-trimethylammoniumethyl carbonate. Two conserved heavy-chain residues, tyrosine(Tyr)-33 and arsinine(Arg)-52, were postulated to be involved in binding and hydrolysis of 4-nitrophenylcholine carbonate esters. To more precisely define the catalytic roles of these residues, 3 Arg-52 mutants (R52K, R52Q, R52C) and 4 Tyr-33 mutants (Y33H, Y33F, Y33E, Y33D) of antibody S107 were generated. The genes encoding the VH binding domain of S107 were inserted into plasmid pUC-f1, and in vitro, mutagenesis was performed. The wild-type and mutant S107 antibodies were expressed in P-3X63-Ag8.653 (P-3) myeloma cells by using a modified SV2 shuttle vector. The catalytic properties of wild-type antibody S107 are similar to those of the phosphocholine- specific antibody T15, which has the same VH protein sequence. In general, mutations at Tyr-33 had little effect on catalytic activity, whereas mutations at Arg-52 that result in loss of the pos. charged side chain significantly lower the catalytic activity of S107. One mutant, Y33H, catalyzed the hydrolysis of 4-nitrophenyl N-trimethylammonioethyl carbonate with a kcat of 5.7 min-1 and a Km of 1.7 mM at pH 7.5. These results not only demonstrate the importance of electrostatic interactions in catalysis by antibody S107 but also show that catalytic side chains can be introduced into antibodies to enhance their catalytic efficiency.

L9 ANSWER 10 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN

1991:77768 Document No. 114:77768 Catalytic antibodies prepared by chemical

modification of the antibody. Schultz, Peter (University of California, Oakland, USA). PCT Int. Appl. WO 9005746 A1 19900531, 100 pp. DESIGNATED STATES: W: AU, DK, FI, JP, KR, SU; RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1989-US5258 19891115. PRIORITY: US 1988-273455 19881118; US 1989-404920 19890908.

AB Antibodies with catalytic properties are prepared by either chemical modification to introduce a reactive group, or the use of reactant or transition state analogs as haptens, or by the introduction of useful amino acids into the protein by site-directed mutagenesis of the gene, followed by chemical modification of the protein. An IgA that binds 2,4-dinitrophenyl (DNP) ligands was modified using DNP affinity labels (e.g. (N-2,4-dinitrophenyl)-2-aminoethyl-3-oxopropyl disulfide, 1-bromo-2-oxo-6-(S-DNP)-mercaptohexane) that were cleaved to leave a thiopyridyl group in the antigen-binding groove of the antibody. The positions of the ligands were confirmed by sequencing. Antibody modified using (N-2,4-dinitrophenyl-2-aminoethyl)-4-oxobutyl disulfide was found to accelerate the hydrolysis of DNP esters 6 + 104-fold over the rate in buffer containing an equimolar concentration of thiol groups (as dithiothreitol). The reaction showed Michaelis-Menten kinetics. The use of analogs as haptens to generate antibodies that catalyze the hydrolysis of thymidine dimers and the generatiojn of an ester hydrolyzing antibody by site-directed mutagenesis were also described.

```
=> S ASP
         29255 ASP
           191 ASPS
L10      29382 ASP
                (ASP OR ASPS)

=> S ASN
         14333 ASN
            85 ASNS
L11      14412 ASN
                (ASN OR ASNS)

=> S L7,L11;S L8 OR L10
L12      43760 (L7 OR L11)


L13      90461 L8 OR L10

=> S L4 AND (L12,L13)
L14         55 L4 AND ((L12 OR L13))

=> S L14 NOT L9
L15         45 L14 NOT L9

=> D 1-45 CBIB ABS
```

L15 ANSWER 1 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN

2006:13229 Document No. 144:101036 Antibody and antisense polynucleotide modulating genes differentially expressed in polycystic disorders for treating polycystic diseases. McPherson, John M.; Beskrovnaya, Oxana (Genzyme Corporation, USA). PCT Int. Appl. WO 2006002203 A2 20060105, 78 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IS, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2005-US21994 20050623. PRIORITY: US 2004-582673P 20040623; US 2004-582875P 20040625.

AB This invention provides compns. and methods to diagnose and treat polycystic disorders by inhibiting the biol. activity of a gene now correlated with appearance of this disorder. By way of illustrative only, the Tissue Growth Factor-alpha (TGF-α) gene is an example of such a gene. Also provided are antibody, antisense polynucleotide,

ribozyme, and multivalent RNA aptamer to treat or ameliorate abnormal cystic lesions and diseases associated with the formation of cysts in tissue. The methods and compns. treat and ameliorate pathol. cyst formation in tissue by inhibiting or augmenting gene expression or the biol. activity the gene expression product, or its receptor.

L15 ANSWER 2 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN
2005:446474 Document No. 144:82952 Site-directed mutagenesis study of the antibody 2D7 which catalyzes a reaction for insertion of Cu2+ into mesoporphyrin. Hosomi, Naoki; Kawamura-Konishi, Yasuko; Kawano, Ryota; Fujii, Ikuo; Suzuki, Haruo (Graduate School of Fundamental Life Science, Kitasato University, Kanagawa, 228-8555, Japan). Journal of Bioscience and Bioengineering, 99(3), 222-229 (English) 2005. CODEN: JBBIF6. ISSN: 1389-1723. Publisher: Society for Biotechnology, Japan.

AB Monoclonal antibody 2D7 generated against a transition-state analog N-Me mesoporphyrin catalyzes a reaction for insertion of a cupric ion into mesoporphyrin. To investigate amino acid residues responsible for the catalytic activity, site-directed mutagenesis of the amino acid residues in the third complementarity determining region of the heavy chain (CDRH3) was performed on the antigen-binding fragment (Fab) of the antibody. Recombinant Fab mutants, in which Arg95 is replaced with Ala (R95A), Asp96 with Asn (D96N) and Met97 with Gly (M97G), were examined in terms of the catalytic efficiency of the reaction (k/KS) and the dissociation constant for N-Me mesoporphyrin binding (Kd) and these values were compared with those of the wild type. The k/KS values of the R95A and D96N mutants were 0.96% and 1.0% of that of the wild type, resp., whereas the M97G mutant had no detectable catalytic activity. The Kd values of the R95A and D96N mutants were 165 and 69 times that of the wild type, resp., while that of the M97G mutant was similar to that of the wild type. The relationship between the k/KS and 1/Kd values in the wild type and the R95A and D96N mutants suggests that Arg95 and Asp96 are responsible for stabilizing the transition-state in the catalytic reaction. The results of the M97G mutant allow us to propose that Met97 plays an important role in the catalytic activity probably due to a subtle and specific conformation of the antibody.

L15 ANSWER 3 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN
2005:353540 Document No. 143:55599 Structural origins of efficient proton abstraction from carbon by a catalytic antibody. Debler, Erik W.; Ito, Shuichiro; Seebeck, Florian P.; Heine, Andreas; Hilvert, Donald; Wilson, Ian A. (Department of Molecular Biology and The Skaggs Institute for Chemical Biology, The Scripps Research Institute, La Jolla, CA, 92037, USA). Proceedings of the National Academy of Sciences of the United States of America, 102(14), 4984-4989 (English) 2005. CODEN: PNASA6. ISSN: 0027-8424. Publisher: National Academy of Sciences.

AB Antibody 34E4 catalyzes the conversion of benzisoxazoles to salicylonitriles with high rates and multiple turnovers. The crystal structure of its complex with the benzimidazolium hapten at 2.5-Å resolution shows that a combination of hydrogen bonding, π stacking, and van der Waals interactions is exploited to position both the base, GluH50, and the substrate for efficient proton transfer. Suboptimal placement of the catalytic carboxylate, as observed in the 2.8-Å structure of the GluH50Asp variant, results in substantially reduced catalytic efficiency. In addition to imposing high positional order on the transition state, the antibody pocket provides a highly structured microenvironment for the reaction in which the carboxylate base is activated through partial desolvation, and the highly polarizable transition state is stabilized by dispersion interactions with the aromatic residue TrpL91 and solvation of the leaving group oxygen by external water. The enzyme-like efficiency of general base catalysis in this system directly reflects the original hapten design, in which a charged guanidinium moiety was strategically used to elicit an accurately positioned functional group in an appropriate reaction environment and suggests that even larger catalytic effects may be achievable by extending this approach to the induction of acid-base pairs capable of bifunctional catalysis.

L15 ANSWER 4 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN
2005:69125 Document No. 142:311895 Mechanistic study of proton transfer and hysteresis in catalytic antibody 16E7 by site-directed mutagenesis and homology modeling. Zheng, Lei; Manetsch, Roman; Woggon,

Wolf-Dietrich; Baumann, Ulrich; Reymond, Jean-Louis (Department of Chemistry and Biochemistry, University of Berne, Bern, CH-3012, Switz.). Bioorganic & Medicinal Chemistry, 13(4), 1021-1029 (English) 2005. CODEN: BMECEP. ISSN: 0968-0896. Publisher: Elsevier Ltd..

AB Antibody 16E7 catalyzes the carbon protonation of enol ether 2 to hemiacetal 3, and the carbon deprotonation of benzisoxazole 7 to phenol 8. This antibody shows an extreme case of hysteresis, requiring several hours to reach full activity. Antibody 16E7 was expressed as recombinant chimeric Fab in Escherichia coli. A model for the three-dimensional structure was produced by homol. modeling and used for a docking procedure to obtain models for antibody-ligand complexes. Site-direct mutagenesis of GluL39, identified as a possible catalytic residue by the model, to either glutamine or alanine abolished catalysis, showing that both the protonation reaction of enol ether 2 and the deprotonation of benzisoxazole 7 are promoted by the same residue. The model furthermore suggested that substrate access to the catalytic site might be hindered by a flexible HCDR3 loop held in closed position by a hydrogen bond between SerH99 and GluL39, which could explain the observed hysteresis effect. In agreement with this model, mutagenesis of SerH99 to alanine, or deletion of this residue, was found to reduce hysteresis by approx. 50%.

L15 ANSWER 5 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN

2004:789852 Document No. 142:311917 Chemical modification of a catalytic antibody that accelerates insertion of a metal ion into porphyrin: essential amino acid residues for the catalytic activity. Kawamura-Konishi, Yasuko; Aoki, Takeshi; Satoh, Nobuyoshi; Katagiri, Masanao; Suzuki, Haruo (Division of Biosciences, Graduate School of Fundamental Life Science, Kitasato University, Sagamihara, Kanagawa, 228-8555, Japan). Journal of Molecular Catalysis B: Enzymatic, 31(1-3), 9-17 (English) 2004. CODEN: JMCEF8. ISSN: 1381-1177. Publisher: Elsevier B.V..

AB Catalytic antibody 2B generated by immunization with N-Me mesoporphyrin as hapten catalyzes the insertion of a cupric ion into mesoporphyrin. To identify amino acid residues essential for the catalytic activity, we studied effects of various amino acid-reactive reagents on the catalytic activity. The reagents reactive to Arg, Tyr and carboxyl-containing residues inactivated the antibody and mesoporphyrin protected notably the antibody from the inactivation. These results indicated that Arg, Tyr and carboxyl-containing residues are situated in or near the substrate-binding site of the antibody and that some of them would be essential for the catalytic activity. The modified Arg and Tyr residues in the inactivation were quantified in connection with the residual activity. As the result, it was shown that three Arg and one Tyr residues are modified to lead the inactivation. Kinetic anal. indicated that the antibody loses the catalytic activity by modification of one carboxyl-containing residue. In order to find candidates for the modified residues, we performed modeling of the variable domain of the antibody. The model showed that the modified residues are Arg L54, Arg H94, Arg H95, Tyr L91 and Asp H96, and suggested that Arg H95, Tyr L91 and Asp H96 residues would stabilize the transition state of mesoporphyrin in the antibody-mediated reaction.

L15 ANSWER 6 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN

2004:553565 Document No. 141:238716 Antibody-Catalyzed Oxy-Cope Rearrangement: Mechanism and Origins of Catalysis and Stereoselectivity from DFT Quantum Mechanics and Flexible Docking. Black, Kersey A.; Leach, Andrew G.; Kalani, M. Yashar S.; Houk, K. N. (Department of Chemistry and Biochemistry, University of California, Los Angeles, CA, 90095-1569, USA). Journal of the American Chemical Society, 126(31), 9695-9708 (English) 2004. CODEN: JACSAT. ISSN: 0002-7863. Publisher: American Chemical Society.

AB D. functional theory using B3LYP and flexible ligand docking methods were used to investigate the complete potential surface for the uncatalyzed and the AZ28 antibody-catalyzed oxy-Cope reaction of 2,5-diaryl-1,5-hexadien-3-ol derivs. The reaction mechanism is stepwise, involving a cyclohexane diyl intermediate. Theor. deuterium isotope effects match well with those from experiment Gas-phase transition structures show mixed preferences for the axial vs equatorial hydroxyl group, while solvation favors the axial isomer. Specific Ph group conformations are shown to be critical to transition-state stabilization (by up to 15 kcal/mol), and the effective conformation is not that found in the hapten used to generate the germline and affinity-matured AZ28

catalytic antibodies. Docking studies support greater transition-state binding than reactant binding. Docking studies also predict the S stereoselectivity of mature AZ28 and suggest that binding modes quite different from those of the hapten might play a role in catalysis, with specific focus on ligand hydrogen bonding to AspH101.

L15 ANSWER 7 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN
2004:445914 Document No. 141:136173 Crystallographic and Biochemical Analysis of Cocaine-Degrading Antibody 15A10. Larsen, N. A.; de Prada, P.; Deng, S.-X.; Mittal, A.; Braskett, M.; Zhu, X.; Wilson, I. A.; Landry, D. W. (Department of Molecular Biology and Skaggs Institute for Chemical Biology, The Scripps Research Institute, La Jolla, CA, USA). Biochemistry, 43(25), 8067-8076 (English) 2004. CODEN: BICHAW. ISSN: 0006-2960. Publisher: American Chemical Society.

AB Catalytic antibody 15A10 hydrolyzes the benzoyl ester of cocaine to form the non-psychoactive metabolites benzoic acid and ecgonine Me ester. Here, we report biochem. and structural studies that characterize the catalytic mechanism. The crystal structure of the cocaine-hydrolyzing monoclonal antibody (mAb) 15A10 has been determined at 2.35 Å resolution The binding pocket is fairly shallow and mainly hydrophobic but with a cluster of three hydrogen-bond donating residues (TrpL96, AsnH33, and TyrH35). Computational docking of the transition state analog (TSA) indicates that these residues are appropriately positioned to coordinate the phosphonate moiety of the TSA and, hence, form an oxyanion hole. Tyrosine modification of the antibody with tetranitromethane reduced hydrolytic activity to background level. The contribution from these and other residues to catalysis and TSA binding was explored by site-directed mutagenesis of 15A10 expressed in a single chain fragment variable (scFv) format. The TyrH35Phe mutant had 4-fold reduced activity, and TrpL96Ala, TrpL96His, and AsnH33Ala mutants were all inactive. Comparison with an esterolytic antibody D2.3 revealed a similar arrangement of tryptophan, asparagine, and tyrosine residues in the oxyanion hole that stabilizes the transition state for ester hydrolysis. Furthermore, the crystal structure of the bacterial cocaine esterase (cocE) also showed that the cocE employs a tyrosine hydroxyl in the oxyanion hole. Thus, the biochem. and structural data are consistent with the catalytic antibody providing oxyanion stabilization as its major contribution to catalysis.

L15 ANSWER 8 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN
2004:251516 Document No. 140:419860 Molecular mechanism of enantioselective proton transfer to carbon in catalytic antibody 14D9. Zheng, Lei; Baumann, Ulrich; Reymond, Jean-Louis (Department of Chemistry and Biochemistry, University of Bern, Bern, CH-3012, Switz.). Proceedings of the National Academy of Sciences of the United States of America, 101(10), 3387-3392 (English) 2004. CODEN: PNASA6. ISSN: 0027-8424. Publisher: National Academy of Sciences.

AB Catalytic antibody 14D9 catalyzes the enantioselective protonation of prochiral enol ethers with high enantioselectivity (>99% ee) and a practical turnover (kcat = 0.4 s-1), allowing for preparative scale applications. This antibody represents one of the rare examples of catalytic antibodies promoting acid-catalyzed processes. Antibody 14D9 was cloned and expressed as a chimeric Fab fragment in Escherichia coli. Crystal structures of Fab 14D9 as apo form and of its close analog 19C9 in complex with the transition state analog were determined at 2.8-Å resolution A series of site-directed mutagenesis expts. was carried out to probe the role of individual active-site amino acids. Proton transfer to carbon is catalyzed by a hydrogen bond network formed by the side chains of AspH101 and TyrL36 with a water mol. serving as a relay. The intermediate oxocarbonium ion formed during the protonation step is trapped by the same water mol., resulting in an overall syn-addition of water to the enol ether's double bond. The enantioselectivity is caused by steric crowding at the active site, mainly because of the side chain of PheH84. The 20-fold lower activity of 19C9 compared with 14D9 was traced down to residue ThrL46, which forms a nonproductive hydrogen bond with the catalytic residue AspH101, which competes with the critical AspH101-TyrL36 hydrogen bond and therefore reduces catalytic efficiency. The catalytic activity of 19C9 was restored to that of 14D9 by using either site-directed mutagenesis (ThrL46Ala) or chain shuffling.

L15 ANSWER 9 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN
2004:80867 Document No. 140:141687 Design of catalytic

antibodies based on analysis of catalytic triads by molecular modeling. Uda, Taizo; Hifumi, Emi (Japan Science and Technology Corporation, Japan). PCT Int. Appl. WO 2004009805 A1 20040129, 232 pp. DESIGNATED STATES: W: US; RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR. (Japanese). CODEN: PIXXD2. APPLICATION: WO 2003-JP9147 20030718. PRIORITY: JP 2002-211756 20020719; JP 2002-211768 20020719; JP 2003-51943 20030227; JP 2003-198270 20030717; JP 2003-198281 20030717; JP 2003-198292 20030717.

AB A process for producing catalytic antibodies which involves an antibody structure anal. step of confirming the presence of a catalytic triad structure wherein a serine residue, an aspartate residue and a histidine residue or a glutamate residue are located sterically or spatially close to each other in the stereostructure of an antibody predicted based on its amino acid sequence. Since the above-described catalytic triad structure is specific to catalytic antibodies, catalytic antibodies can be efficiently screened by using the same. Examples of the antibody enzyme as described above include catalytic antibodies against Helicobacter pylori urease and catalytic antibodies against human chemokine receptor CCR-5. A monoclonal antibody i41SL1-2 raised against the a highly conserved peptide sequence of complementarity determining region-1 (CDRL-1) of super catalytic antibody, 41S-2-L, which is capable of enzymically destroying the gp41 mol. of HIV-1 envelope, was prepared From mol. modeling, the light and heavy chains of the antibody were deduced to possess catalytic triads (Asp, His, and Ser) in their steric conformations, which may be responsible for the observed proteolytic activity. Helicobacter pylori (H. pyroli) causes chronic gastritis and gastric ulcer. The authors have established a unique monoclonal antibody which has a specificity against H. pyroli urease. Computer program.

L15 ANSWER 10 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN

2003:856097 Document No. 139:346752 Walk-through mutagenesis for mutation of amino acid in target regions of polypeptide of interest. Crea, Roberto; Cappuccilli, Guido (USA). PCT Int. Appl. WO 2003089671 A1 20031030, 40 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-US11935 20030416. PRIORITY: US 2002-2002/PV373686 20020417.

AB A method of walk-through mutagenesis of a nucleic acid encoding a prototype polypeptide of interest, is described. The method comprises selecting a predetd. amino acid and one or more target regions of the polypeptide, and synthesizing a mixture of oligonucleotides containing at each sequence position in the target region, either a prototype nucleotide that is required for synthesis of the prototype amino acid of the polypeptide, or a predetd. nucleotide that is required for synthesis of the predetd. amino acid, in which during the synthesis, the ratio of available prototype nucleotides, to available predetd. nucleotides, is greater than 1:1. The method is based on the premise that certain amino acids play crucial roles in the structure and function of proteins. Libraries can be generated which contain a high proportion of the desired mutants and are of reasonable size for screening. This libraries can be used to study the role of specific amino acids in protein structure and function and to develop new or improved proteins and polypeptides such as antibodies, Ig and catalytic antibodies. The method involves synthesizing a mixture of oligonucleotides containing all variant sequences of the region of interest, which are then used for synthesis of the mutant proteins.

L15 ANSWER 11 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN

2003:688299 Document No. 140:352571 Key residue responsible for catalytic activities in the antibodies elicited against N-methyl mesoporphyrin. Kawamura-Konishi, Yasuko; Sasaki, Rumie; Sugiyama, Masami; Hashimoto, Hiroshi; Kamo, Takako; Hosomi, Naoki; Yamazaki, Masaaki; Tashiro, Hiroyuki; Suzuki, Haruo (School of Science, Department of Biosciences, Kitasato University, Sagamihara, Kanagawa, 228-8555, Japan). Journal of Molecular Catalysis B: Enzymatic, 24-25, 99-109 (English) 2003. CODEN: JMCEF8. ISSN: 1381-1177. Publisher:

Elsevier Science B.V..

AB Five catalytic and nine non-catalytic antibodies for insertion of a metal ion into porphyrin were generated by immunization with N-Me mesoporphyrin (N-MMP) as hapten, which was designed to mimic the distortion of porphyrin toward a transition-state geometry in the reaction. In order to determine the features responsible for the catalytic activity, we characterized the properties of the catalytic and non-catalytic antibodies. The catalytic antibodies did not have higher affinity to N-MMP than the non-catalytic ones. All the antibodies, except one non-catalytic antibody, combined with ferric N-Me mesoporphyrin (N-MMP-Fe) to form the resp. antibody·N-MMP-Fe complex. The binding affinity of cyanide to ferric iron in the complexes agreed with that of free N-MMP-Fe, indicating that the protruding side of N-MMP-Fe in the complexes is exposed to solvents. All the complexes of the catalytic antibodies had a peroxidase-like activity, whereas those of the non-catalytic ones did not. This suggests that the metalation activity assocs. with the peroxidase-like one, so that there is a common residue acting as catalyst for both reactions. The amino acid sequence alignment shows that the catalytic antibodies contain a homologous heavy chain sequence in the third complementarity-determining region (CDR). Based on the results, the possibility that Asp(H96) in the region is the key residue responsible for the metalation and peroxidase-like activities is discussed.

L15 ANSWER 12 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN

2003:293885 Document No. 139:242180 Endopeptidase character of monoclonal antibody i41-7 subunits. Hatiuchi, Kenji; Hifumi, Emi; Mitsuda, Yukie; Uda, Taizo (School of Biosciences, Hiroshima Prefectural University, Shobara City, 727-0023, Japan). Immunology Letters, 86(3), 249-257 (English) 2003. CODEN: IMLED6. ISSN: 0165-2478. Publisher: Elsevier Science Ireland Ltd..

AB We prepared six anti-idiotypic monoclonal antibodies (mAbs) against parent 41S-2 mAb whose light chain is a super catalytic antibody (41S-2-L) capable of degrading targeted HIV-1gp41 mol. Out of the obtained six mAbs, i41-7 mAb showed the strongest affinity to the parent 41S-2 mAb. The three dimensional structure of i41-7 mAb was created by mol. modeling using the deduced amino acid sequence of the light and heavy chain of i41-7 mAb. It suggests that the light and heavy chain possess catalytic triad-like structure composed of Ser, His and Asp in their conformations. Both chains of i41-7 mAb could cleave peptide bond of some peptides such as a polypeptide, TP41-1 (TPRGPDRPEGIEEEGGERDRD), as anticipated. The cleaving reaction advanced in accordance with Michaelis-Menten equation. The catalytic efficiency (kcat/Km) of light and heavy chain was 9.1+103 and 1.7+104 M-1 min-1, resp., while the intact i41-7 mAb did not exhibit any catalytic activity. The first cleaved bond of the TP41-1 peptide by the light chain was between 14E and 15G in the sequence. It was revealed that both light and heavy chains had endopeptidase characteristics.

L15 ANSWER 13 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN

2003:110325 Document No. 138:299686 Experimental Determination of the Absolute Enantioselectivity of an Antibody-Catalyzed Diels-Alder Reaction and Theoretical Explorations of the Origins of Stereoselectivity. Cannizzaro, Carina E.; Ashley, Jon A.; Janda, K. D.; Houk, K. N. (Department of Chemistry and Biochemistry, University of California, Los Angeles, CA, 90095-1569, USA). Journal of the American Chemical Society, 125(9), 2489-2506 (English) 2003. CODEN: JACSAT. ISSN: 0002-7863. OTHER SOURCES: CASREACT 138:299686. Publisher: American Chemical Society.

AB The exo and endo Diels-Alder adducts of p-methoxycarbonylbenzyl trans-1,3-butadiene-1-carbamate and N,N-dimethylacrylamide have been synthesized, and the absolute configurations of resolved enantiomers have been determined On the basis of this information, the absolute enantioselectivities of the Diels-Alder reaction catalyzed by antibodies 13G5 and 4D5 as well as other catalytic antibodies elicited in the same immunizations have been established. The effects of different arrangements of catalytic residues on the structure and energetics of the possible Diels-Alder transition states were modeled quantum mech. at the B3LYP/6-311++G**//B3LYP/6-31+G** level of theory. Flexible docking of these enantiomeric transition states in the antibody active site followed by mol. dynamics on the resulting complexes provided a prediction of the transition-state binding modes and an explanation of the origin of the observed enantioselectivity of antibody 13G5.

L15 ANSWER 14 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN
2002:858661 Document No. 138:133076 Presence of catalytic activity of the antibody light chain raised against complementarity determining region peptide of super catalytic antibody . Zhou, Y.; Hifumi, E.; Kondo, H.; Uda, T. (Department of Biosciences, Hiroshima Prefectural University, Shobara City, 727-0023, Japan). ACS Symposium Series, 830(Biological Systems Engineering), 200-208 (English) 2002. CODEN: ACSMC8. ISSN: 0097-6156. Publisher: American Chemical Society.

AB A monoclonal antibody i41SL1-2 raised against the peptide of complementarity determining region-1 (CDRL-1) of super catalytic antibody, 41S-2-L, which is capable of enzymically destroying the gp41 mol. of HIV-1 envelope, was prepared The light chain, i41SL1-2-L, catalytically decomposed the CDRL-1 peptide through the successive reaction. Based on the mol. modeling, i41SL1-2 possesses a catalytic triad composed of Ser, His, Asp, whose positions are identical to those of the catalytic antibody, VIPase.

L15 ANSWER 15 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN
2002:787396 Document No. 138:51878 New variation on a theme: structure and mechanism of action of hydrolytic antibody 7F11, an aspartate rich relation of catalytic antibodies 17E8 and 29G11.
Cross, Simon S. J.; Brady, Kevin; Stevenson, James D.; Sackin, Jenny R.; Kenward, Nigel; Dietel, Anja; Thomas, Neil R. (School of Chemistry, University of Nottingham, Nottingham, NG7 2RD, UK). Journal of Immunological Methods, 269(1-2), 173-195 (English) 2002. CODEN: JIMMBG. ISSN: 0022-1759. Publisher: Elsevier Science B.V..

AB A computer model, based on homol., of the catalytic antibody 7F11 that catalyzes the decomposition of the benzoate ester of a dioxetane resulting in chemiluminescence is reported. Antibody 7F11 has 89% identity in the VL domain, and 72% identity in the VH domain with hydrolytic antibodies 17E8 and 29G11 previously reported by Scanlan et al. These were also raised against a phosphonate containing hapten. The antigen-binding site of antibody 7F11 while similar to that of 17E8 has aspartic acids at positions 33H and 35H, reminiscent in position of the catalytic residues found in aspartate proteinases such as pepsin. AutoDock 3.0 has been used to identify the best binding mode for the hapten. Mol. dynamic simulations have also been undertaken to examine any major conformational changes induced by hapten binding. A mechanism for benzoate ester hydrolysis involving the aspartic acid side-chains is proposed. Construction of a single-chain variable fragment (scFv) of 7F11 is also reported.

L15 ANSWER 16 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN
2002:520720 Document No. 138:1424 Enzymatic characterization of glycosidase antibodies raised against a chair transition state analog and the retained catalytic activity from the expressed single chain antibody fragments.
Choi, So-Young; Youn, Hyun Joo; Yu, Jaehoon (Life Sciences Division, The Korea Institute of Science and Technology, Seoul, 130-650, S. Korea). Molecules and Cells, 13(3), 463-469 (English) 2002. CODEN: MOCEEK. ISSN: 1016-8478. Publisher: Springer-Verlag Singapore Pte. Ltd..

AB Catalytic antibodies with a glycosidase activity have been generated against a chair-like transition state analog. Two monoclonal antibodies with the highest activity were selected for cloning and sequencing. Sequence anal. of the two antibodies showed four amino acids differences in the framework region. Such a difference resulted in 8-fold difference in catalytic activity with p-nitrophenyl-β-D- glucopyranoside between the two antibodies. Several Asp and Glu residues were found in the complementarity determining region and some of these residue(s) might form the catalytic core for the glycosidase. Cloned antibody genes were expressed as a single chain antibody fragment. The expressed proteins showed the retained glycosidase activities.

L15 ANSWER 17 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN
2002:450256 Document No. 137:2733 Ion-exchange resin / enzyme activity assay. Karsten, Thomas P.; Currie, Mark G.; Moore, William M. (Pharmacia Corporation, USA). U.S. Pat. Appl. Publ. US 2002072082 A1 20020613, 7 pp. (English). CODEN: USXXCO. APPLICATION: US 2001-888008 20010622.

PRIORITY: US 2000-2000/PV213354 20000622.

AB The present invention relates to a rapid high-throughput ion-exchange resin assay for determining enzyme activity. This novel assay uses a radiometric technique which separates the radioactive substrate from the product (or the radioactive product from the substrate) by exploiting the differences in the net charges of the mols. using ion-exchange resin. This assay is useful, for example, for studies of enzyme kinetics, the identification of functional sites in the enzyme, and in the automated screening of compound libraries for pharmaceutical drug development.

L15 ANSWER 18 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN

2002:45333 Document No. 137:4732 Computational 3-D modeling and site-directed mutation of an antibody that binds Neu2en5Ac, a transition state analogue of a sialic acid. Kamei, Hiroya; Shimazaki, Kazuko; Nishi, Yoshisuke (Laboratory of Life Science & Biomolecular Engineering, Japan Tobacco Inc., Yokohama, 227-8512, Japan). Proteins: Structure, Function, and Genetics, 45(4), 285-296 (English) 2001. CODEN: PSFGEY. ISSN: 0887-3585. Publisher: Wiley-Liss, Inc..

AB An antibody against a transition state analog (TSA) may share some common features with an enzyme that produces such a transition state. SIC172 antibody binds specifically to Neu2en5Ac, a TSA of Neu5Ac in the sialidase reaction, but has no catalytic activity. To understand how the antibody recognizes Neu2en5Ac and to find out if it is possible to convert it to a catalytic antibody, the authors made and sequenced the SIC172 ScFv, and constructed a 3-D model of it. The VH-CDR3 contains a unique sequence with Cys at H95. The 3-D model showed that Cys-H95 is exposed inside the antigen-binding cavity. After affinity docking, 4 types emerged. In type I, the carboxyl group of Neu2en5Ac is located near the Cys-H95 and neighboring pos. charged residues. The change of Cys-H95 to Asp by site-directed mutation decreased the binding activity, while a change to Arg did not. These and other mutation expts., and further modeling of mutant Fv, support the 3-D model and docking type I. A comparison with sialidase indicates that SIC172 antibody appears to have some groups of residues that are conserved at the active site of the enzyme. The possibility of Neu2en5Ac-binding antibody being converted to a catalytic antibody is discussed.

L15 ANSWER 19 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN

2001:254151 Document No. 135:15947 Computer modeling on abzyme catalyzing soman hydrolysis. Hu, Yuandong; Zheng, Zhibin; Wang, Ziling; Jiao, Kefang; Rong, Kangtai; Li, Song (Beijing Institute of Pharmacology and Toxicology, Beijing, 100850, Peop. Rep. China). Zhongguo Yaolixue Yu Dulixue Zazhi, 15(1), 60-64 (Chinese) 2001. CODEN: ZYYZEW. ISSN: 1000-3002. Publisher: Zhongguo Yaolixue Yu Dulixue Zazhi Biarjibu.

AB The PRCR-soman was docked into the active sites of variable region of abzyme EP6 (EP6V) using the automated flexible docking procedure (Affinity), the complex structure of soman-EP6V and the interaction energy between soman and EP6V showed that H-bond and electrostatic interaction were important. The residues of the heavy chain Asn 52 and light chain Tyr 95 played key role in the process of the soman hydrolysis, and water mol. was also important in this process under the physiol. conditions.

L15 ANSWER 20 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN

2000:336502 Document No. 133:118705 How and why 41S-2 antibody subunits acquire the ability to catalyze decomposition of the conserved sequence of gp41 of HIV-1. Hifumi, Emi; Okamoto, Yoshiko; Uda, Taizo (School of Biosciences, Hiroshima Prefectural University, Hiroshima, 727-0023, Japan). Applied Biochemistry and Biotechnology, 83(1-3), 209-220 (English) 2000. CODEN: ABIBDL. ISSN: 0273-2289. Publisher: Humana Press Inc..

AB It has become well known that antibodies obtained by immunization with the ground state of peptides can display proteolytic activity. Our antibody light chain produced by immunization with the peptide RGPDRPEGIEEEGGERDRD, a highly conserved sequence in envelope gp41 of HIV-1 showed the ability to cleave this peptide. Moreover, its heavy chain also decomposed the peptide, although this occurred at lower activity levels compared with the light chain, while the whole antibody did not show any catalytic activity. From mol. modeling, the light and heavy chains of the antibody were deduced to possess catalytic triads (Asp, His, and Ser) in their steric conformations, which may be responsible for the observed proteolytic activity.

L15 ANSWER 21 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN
2000:226806 Document No. 133:39808 Mechanism of an antibody-catalysed allylic isomerization. Goncalves, Olivier; Dintinger, Thierry; Lebreton, Jacques; Blanchard, Dominique; Tellier, Charles (UPRES no. 2161 "Biocatalyse", Faculte des Sciences et des Techniques, Nantes, 44322, Fr.). Biochemical Journal, 346(3), 691-698 (English) 2000. CODEN: BIJOAK. ISSN: 0264-6021. Publisher: Portland Press Ltd..

AB The catalytic antibody 4B2, which was generated against a substituted amidine, catalyzes the allylic isomerization of β,γ-unsatd. ketones with an acceleration factor (kcat/kuncat) of 1.5 + 103. On the basis of the "bait and switch" strategy, it was reasoned that the pos. charged hapten could elicit, by charge complementarity, an acidic residue (Asp or Glu) in the antibody-binding site in the right position to catalyze this proton transfer reaction. The pH dependence curve of kcat/Km shows a bell-shaped feature with an optimum at approx. pH 4.5. By cloning and sequencing the light and heavy chains of the 4B2 antibody, we confirmed the presence of several Asp and Glu residues in the complementarity-determining region loops. The antibody catalyzes the α-proton exchange on the same substrates, demonstrating the involvement of a dienol intermediate in the reaction mechanism. Kinetic studies with 2H-NMR provide evidence that α-proton abstraction is stereospecific. Whether the process involves one or two acid/base residues in this simple proton transfer or whether it is a concerted mechanism is discussed.

L15 ANSWER 22 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN
2000:185457 Document No. 132:344728 Innate antibody catalysis. Gololobov, Gennady; Sun, Mei; Paul, Sudhir (Department of Pathology and Laboratory Medicine, University of Texas Medical School, Houston, TX, 77030, USA). Molecular Immunology, Volume Date 1999, 36(18), 1215-1222 (English) 2000. CODEN: MOIMD5. ISSN: 0161-5890. Publisher: Elsevier Science Ltd..

AB Catalysis by antibodies is often assumed to require immunization with artificial haptens, which are proposed to stimulate adaptive immune processes and enable the development of catalytic sites with the ability to bind the transition state. Contrary to this assumption, we describe here a serine protease-like catalytic triad in an antibody light chain raised by immunization with vasoactive intestinal peptide (VIP), the structure and function of which is inherited via a germline VL gene. The serine protease mechanism was evident from loss of the catalytic activity by site directed mutagenesis at a framework region residue Asp1 (present study) and at two complementarity determining region residues Ser27a and His 93. All three catalytic residues (Ser27a, His93, Asp1) are also present in the germline counterpart of the mature VL gene, but the mature and germline sequences differ by four amino acids remote from the catalytic site. Reversion mutations were introduced at these amino acids in the mature light chain (His27 d:Asp, Thr28e:Ser, Ile34:Asn, Gln96:Trp; Kabat numbering, germline encoded residues shown second), generating the germline configuration of the protein. The germline light chain expressed peptidase activity, determined by assaying the cleavage of VIP and a synthetic protease substrate, Pro-Phe-Arg-Methylcoumarinamide. Differences between the kinetic consts. for the mature and germline light chains were marginal. Diisopropylfluorophosphate, a serine protease inhibitor, blocked the peptidase activity of the germline light chain, suggesting the presence of the catalytic triad in a functional state. Like the mature light chain, the germline protein preferentially cleaves peptide bonds on the C-terminal side of basic residues. We conclude that the catalytic activity of certain antibodies is an innate function, originating over the course of phylogenetic evolution of the VL genes, as opposed to somatic processes.

L15 ANSWER 23 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN
1999:294275 Document No. 131:127147 Structural Basis for Antibody Catalysis of a Disfavored Ring Closure Reaction. Gruber, Karl; Zhou, Bin; Houk, Kendall N.; Lerner, Richard A.; Shevlin, Charles G.; Wilson, Ian A. (Departments of Molecular Biology and Chemistry and the Skaggs Institute for Chemical Biology, The Scripps Research Institute, La Jolla, CA, 92037, USA). Biochemistry, 38(22), 7062-7074 (English) 1999. CODEN: BICHAW. ISSN: 0006-2960. Publisher: American Chemical Society.

AB The catalysis of disfavored chemical reactions, especially those with no known natural enzyme counterparts, is one of the most promising achievements of catalytic antibody research. Antibodies 5C8, 14B9, 17F6, and 26D9, elicited by two different transition-state analogs, catalyze disfavored endo-tet cyclization reactions of trans-epoxy alcs., in formal violation of Baldwin's rules for ring closure. Thus far, neither chemical nor enzyme catalysis has been capable of emulating the extraordinary activity and specificity of these antibodies. X-ray structures of two complexes of Fab 5C8 with the original hapten and with an inhibitor have been determined to 2.0 Å resolution The Fab structure has an active site that contains a putative catalytic diad, consisting of AspH95 and HisL89, capable of general acid/base catalysis. The stabilization of a pos. charge that develops along the reaction coordinate appears to be an important factor for rate enhancement and for directing the reaction along the otherwise disfavored pathway. Sequence anal. of the four catalytic antibodies, as well as four inactive antibodies that strongly bind the transition-state analogs, suggests a conserved catalytic mechanism. The occurrence of the putative base HisL89 in all active antibodies, its absence in three out of the four analyzed inactive antibodies, and the rarity of a histidine at this position in Igs support an important catalytic role for this residue.

L15 ANSWER 24 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN

1999:289407 Document No. 130:322331 Catalytic antibodies which hydrolyze primary amides and methods for eliciting such antibodies. Napper, Andrew D.; Titmas, Richard C.; Martin, Mark T.; Hong, Wonpyo (IGEN International, Inc., USA). U.S. US 5900237 A 19990504, 32 pp., Cont.-in-part of U.S. Ser. No. 52,490. (English). CODEN: USXXAM. APPLICATION: US 1996-362470 19960504. PRIORITY: US 1983-556016 19831129; US 1984-674253 19841127; US 1988-190271 19880504; US 1988-190271 19880504; US 1990-498225 19900323; US 1991-700210 19910612; US 1991-740501 19910805; US 1991-776186 19910903; US 1991-773042 19911010; US 1993-52490 19930423; WO 1994-US4437 19940422.

AB Described and claimed are compds. of formula R1YNHCHR2X, wherein Y is a polypeptide, R1 is bonded to the N-terminus of Y and is hydrogen or a branched or linear, substituted or unsubstituted, C1-21 alkyl, alkene, or alkyne group, R2 is a side chain of a naturally occurring amino acid, and X is -P(OH)CH3, -P(OH)OCH3, or -COCF3. The invention is exemplified by the design and synthesis of such compds. which are useful as haptens and immunogens for the elicitation of antibodies which catalytically enhance the rate of formation or hydrolysis of primary amide bonds. The compds. and catalytic antibodies are useful in the industrial synthesis of amidated peptides of therapeutic value. One of many therapeutic targets are antibodies that hydrolyze the asparagine or glutamine side-chain in peptides.

L15 ANSWER 25 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN

1999:29411 Document No. 130:193612 Probing the importance of second sphere residues in an esterolytic antibody by phage display. Arkin, Michelle R.; Wells, James A. (Department of Protein Engineering, Genentech, Inc., South San Francisco, CA, 94080, USA). Journal of Molecular Biology, 284(4), 1083-1094 (English) 1998. CODEN: JMOBAK. ISSN: 0022-2836. Publisher: Academic Press.

AB We have used phage display to generate a panel of closely related catalytic antibodies. Seeking to improve the catalytic activity of an esterolytic antibody, we displayed libraries derived from the humanized Fab fragment of the antibody 17E8 (h17E8) on filamentous phage and sorted for binding to an immobilized transition-state analog (TSA). Previous work had suggested that residues outside the antibody active site contribute to TSA binding and catalytic efficiency, and we tested this notion by generating libraries containing such "second sphere" residues. Selected variants of h17E8 retained esterolytic activity and showed variations in affinity within 40-fold and kinetic parameters within tenfold of wild-type antibody, indicating that residues remote from the active site do modulate catalytic activity. In order to understand which mutations were responsible for the properties of phage-selected variants, we designed a series of site-directed mutants. From this series, we identified a double mutant in which Tyr97 was changed to Arg in the heavy chain (Y97HR) and the heavy chain Tyr100a was mutated to Asn (Y100aHN). This variant showed a tenfold improvement in catalytic efficiency (kcat/KM) relative to wild-type h17E8. These mutations were additive; Y97HR increases the catalytic turnover (kcat) by three- to four-fold, while Y100aHN has been shown to lower the Michaelis constant (KM) by three- to five-fold.

TSA binding was correlated with catalytic turnover for variants that differed by single mutations, but less so for variants that differed by many mutations. Thus, future selections based on TSA binding should focus on mutating a small number of residues at a time. (c) 1998 Academic Press.

L15 ANSWER 26 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN
1998:572250 Document No. 129:185069 Walk-through mutagenesis for mutation of each position in an amino acid sequence of interest. Crea, Roberto (USA). U.S. US 5798208 A 19980825, 33 pp., Cont.-in-part of U.S. Ser. No. 505,314, abandoned. (English). CODEN: USXXAM. APPLICATION: US 1992-930600 19921102. PRIORITY: US 1990-505314 19900405.

AB A method of mutagenesis by which a predetd. amino acid is introduced into each and every position of a selected set of positions in a preselected region (or several different regions) of a protein to produce library of mutants. The method is based on the premise that certain amino acids play crucial roles in the structure and function of proteins. Libraries can be generated which contain a high proportion of the desired mutants and are of reasonable size for screening. This libraries can be used to study the role of specific amino acids in protein structure and function and to develop new or improved proteins and polypeptides such as enzymes, antibodies, single chain antibodies and catalytic antibodies. The method involves synthesizing a mixture of oligonucleotides containing all variant sequences of the region of interest, which are then used for synthesis of the mutant proteins.

L15 ANSWER 27 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN
1998:209108 Document No. 129:2068 A glycosidase antibody elicited against a chair-like transition state analog by in vitro immunization. Yu, Jaehoon; Choi, So Young; Moon, Kyung-Duk; Chung, Hyun-Ho; Youn, Hyun Joo; Jeong, Sunjoo; Park, Hokoon; Schultz, Peter G. (Division Applied Science, Korea Institute Science Technology, Seoul, 131-791, S. Korea). Proceedings of the National Academy of Sciences of the United States of America, 95(6), 2880-2884 (English) 1998. CODEN: PNASA6. ISSN: 0027-8424. Publisher: National Academy of Sciences.

AB Antibodies were generated against the pos. charged chair-like glycosidase inhibitor nojirimycin by in vitro immunization. A number of catalytic antibodies were isolated, one of which catalyzes the hydrolysis of p-nitrophenyl β-D-glucopyranoside with a rate enhancement (kcat/kuncat) of 105 M over the HOAC-catalyzed reaction. The antibody discriminates modifications in the pyranoside ring of substrate at the C2, C4, and the anomeric positions. The pH dependence of the reaction and chemical modification studies suggest the presence of an active-site Asp or Glu residue that may function as a general acid. This study further defines those requirements necessary to generate antibodies that efficiently cleave glycosidic bonds.

L15 ANSWER 28 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN
1998:39413 Document No. 128:214902 Crystal structure of a catalytic antibody with a serine protease active site. Zhou, G. Wayne; Guo, Jincan; Huang, Wei; Fletterick, Robert J.; Scanlan, Thomas S. (Dep. of Biochem. and Biophys. and Dep. of Pharmaceutical Chem., Univ. of California, San Francisco, CA, 94143, USA). Science (Washington, D. C.), 265(5175), 1059-1064 (English) 1994. CODEN: SCIEAS. ISSN: 0036-8075. Publisher: American Association for the Advancement of Science.

AB The three-dimensional structure of an unusually active hydrolytic antibody with a phosphonate transition state analog (hapten) bound to the active site has been solved to 2.5 Å resolution The antibody (17E8) catalyzes the hydrolysis of norleucine and methionine Ph esters and is selective for amino acid esters that have the natural α-carbon L configuration. A plot of the pH-dependence of the antibody-catalyzed reaction is bell-shaped with an actively maximum at pH 9.5; expts. on mechanism lend support to the formation of a covalent acyl-antibody intermediate. The structural and kinetic data are complementary and support a hydrolytic mechanism for the antibody that is remarkably similar to that of the serine proteases. The antibody active site contains a Ser-His dyad structure proximal to the phosphorous atom of the bound hapten that resembles two of the three components of the Ser-His-Asp catalytic triad of serine proteases. The antibody active site also contains a Lys residue to stabilize oxyanion formation, and a hydrophobic binding pocket for specific substrate recognition of

norleucine and methionine side chains. The structure identifies active site residues that mediate catalysis and suggests specific mutations that may improve the catalytic efficiency of the antibody. This high resolution structure of a catalytic antibody - hapten complex shows that antibodies can converge on active site structures that have arisen through natural enzyme evolution.

L15 ANSWER 29 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN
1997:624985 Document No. 127:304603 Phage display of a catalytic antibody to optimize affinity for transition-state analog binding. Baca, Manuel; Scanlan, Thomas S.; Stephenson, Robert C.; Wells, James A. (Department of Protein Engineering, Genentech, Inc., South San Francisco, CA, 94080, USA). Proceedings of the National Academy of Sciences of the United States of America, 94(19), 10063-10068 (English) 1997. CODEN: PNASA6. ISSN: 0027-8424. Publisher: National Academy of Sciences.

AB Catalytic antibodies have shown great promise for catalyzing a tremendously diverse set of natural and unnatural chemical transformations. However, few catalytic antibodies have efficiencies that approach those of natural enzymes. In principle, random mutagenesis procedures such as phage display could be used to improve the catalytic activities of existing antibodies ; however, these studies have been hampered by difficulties in the recombinant expression of antibodies. Here, we have grafted the antigen binding loops from a murine-derived catalytic antibody , 17E8, onto a human antibody framework in an effort to overcome difficulties associated with recombinant expression and phage display of this antibody. "Humanized" 17E8 retained similar catalytic and hapten binding properties as the murine antibody while levels of functional Fab displayed on phage were 200-fold higher than for a murine variable region/human constant region chimeric Fab. This construct was used to prepare combinatorial libraries. Affinity panning of these resulted in the selection of variants with 2-8-fold improvements in binding affinity for a phosphonate transition-state analog. Surprisingly, none of the affinity-matured variants was more catalytically active than the parent antibody and some were significantly less active. By contrast, a weaker binding variant was identified with 2-fold greater catalytic activity and incorporation of a single substitution (Tyr-100aH → Asn) from this variant into the parent antibody led to a 5-fold increase in catalytic efficiency. Thus, phage display methods can be readily used to optimize binding of catalytic antibodies to transition-state analogs, and when used in conjunction with limited screening for catalysis can identify variants with higher catalytic efficiencies.

L15 ANSWER 30 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN
1997:479447 Document No. 127:202009 X-ray structures of a hydrolytic antibody and of complexes elucidate catalytic pathway from substrate binding and transition state stabilization through water attack and product release. Gigant, Benoit; Charbonnier, Jean-Baptiste; Eshhar, Zelig; Green, Bernard S.; Knossow, Marcel (Laboratoire Enzymologie Biochimie Structurales, Unite Propre Recherche 9063, Centre National Recherche Scientifique, Gif sur Yvette, 91198, Fr.). Proceedings of the National Academy of Sciences of the United States of America, 94(15), 7857-7861 (English) 1997. CODEN: PNASA6. ISSN: 0027-8424. Publisher: National Academy of Sciences.

AB The x-ray structures of the unliganded esterase-like catalytic antibody D2.3 and its complexes with a substrate analog and with one of the reaction products are analyzed. Together with the structure of the phosphonate transition state analog hapten complex, these crystal structures provide a complete description of the reaction pathway. At alkaline pH, D2.3 acts by preferential stabilization of the neg. charged oxyanion intermediate of the reaction that results from hydroxide attack on the substrate. A tyrosine residue plays a crucial role in catalysis; it activates the ester substrate and, together with an asparagine , it stabilizes the oxyanion intermediate. A canal allows facile diffusion of water mols. to the reaction center that is deeply buried in the structure. Residues bordering this canal provide targets for mutagenesis to introduce a general base in the vicinity of the reaction center.

L15 ANSWER 31 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN
1995:919644 Potential substrates for deamidating catalytic antibodies. Liotta, L. J.; Barbella, G. A.; Pelletier, D.

(Department Chemistry, Stonehill College, N. Easton, MA, 02357, USA). Book of Abstracts, 210th ACS National Meeting, Chicago, IL, August 20-24, Issue Pt. 1, CHED-126. American Chemical Society: Washington, D. C. (English) 1995. CODEN: 61XGAC.

AB Nonbiol. essential reactions need a catalyst because there are no enzymes present that are able to recognize the reactants. A solution to this problem can be found in the immune system. The immune system can create an antibody to almost anything. If these antibodies could catalyze biochem. reactions, they would be very useful in studying proteins, biotechnol., and medicine. Some medical uses of catalytic antibodies are the synthesis of drugs such as anti-cancer and anti-AIDS therapies, breaking up protein in blood clots, and vaccines. The main objective of my research is to synthesize the tripeptide Glycine-Asparagine -Phenylalanine, and use the tripeptide as a substrate to test the catalytic ability of certain antibodies that have already been produced. The progress towards the synthesis of this peptide along with spectral characterization will be reported.

L15 ANSWER 32 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN

1995:520851 Document No. 123:28478 Antibody-Catalyzed Rearrangement of a Peptide Bond: Mechanistic and Kinetic Investigations. Liotta, Louis J.; Gibbs, Richard A.; Taylor, Scott D.; Benkovic, Patricia A.; Benkovic, Stephen J. (Department of Chemistry, Pennsylvania State University, University Park, PA, 16802, USA). Journal of the American Chemical Society, 117(17), 4729-41 (English) 1995. CODEN: JACSAT. ISSN: 0002-7863. Publisher: American Chemical Society.

AB Catalysis of the deamidation of asparagine residues may provide a powerful method for the deactivation of proteins. Catalytic antibodies (Gibbs et al. Science 1992, 258, 803) have been induced that catalyze the deamidation of a model dipeptide through an intermediate succinimide. Investigations of the mechanistic characteristics of two such antibodies, RG2-23C7 and RG2-2E4, revealed their ability to accelerate the hydrolysis of either the R- or S-enantiomers of the succinimide by factors of 10-500-fold to yield differing ratios of the aspartate and isoaspartate products. The mixed product ratios imply that two tetrahedral binding sites of unequal effectiveness were induced in response to the tetrahedral mimics (a phosphinate or secondary hydroxyl) within the hapten structure. The antibody RG2-2E4 also catalyzes the deamidation of either the D- or L-asparagine within the dipeptide through the intermediate cyclic imide, resulting in a multistep reaction sequence featuring a series of tetrahedral transition states. The pH-rate profiles do not implicate functional groups within the antibodies' combining sites for either the deamidation or hydrolytic reactions. The strategy of bifunctional or higher order transition state mimics should provide a route to developing catalytic antibodies for reactions requiring multistep processing.

L15 ANSWER 33 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN

1995:411812 Document No. 122:181973 Mechanistically different catalytic antibodies obtained from immunization with a single transition-state analog. Guo, Jincan; Huang, Wei; Zhou, G. Wayne; Fletterick, Robert J.; Scanlan, Thomas S. (Dep. of Pharmaceutical Chemistry, Univ. of California, San Franscisco, CA, 94143-0446, USA). Proceedings of the National Academy of Sciences of the United States of America, 92(5), 1694-8 (English) 1995. CODEN: PNASA6. ISSN: 0027-8424. Publisher: National Academy of Sciences.

AB The variable-region peptide sequence and steady-state kinetic behavior are compared for a family of catalytic antibodies that arose from the same immune response to a transition-state analog. The crystal structure of the most catalytically active member of the family (17E8) has been solved to 2.5 Å resolution and shows that the antibody active site contains a SerH99-HisH35 (H = heavy chains) catalytic dyad analogous to the Ser-His-Asp catalytic triad of serine proteases. The variable-region peptide sequence of the next most active antibody (29G11) differs from that of 17E8 by nine heavy-chain point mutations, and results from computer modeling suggest that the three-dimensional structure of 29G11 is similar to that of 17E8. In addition, 29G11 is an efficient catalytic antibody; it possess 26% of the hydrolytic activity of 17E8. There is one active-site mutation in 29G11 compared to 17E8: position 99 of the heavy chain of 29G11 contains a glycine residue in place of the nucleophilic serine at this position in 17E8. Consistent with this mutation, results from pH-rate studies and hydroxylamine partitioning expts. indicate that in contrast to the catalytic mechanism of 17E8, the mechanism of 29G11-catalyzed electrolysis does not feature nucleophilic catalysis.

L15 ANSWER 34 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN
1995:356841 Document No. 122:131017 Catalytic antibodies which hydrolyze primary amides and methods for eliciting such antibodies. Napper, Andrew D.; Titmas, Richard C.; Martin, Mark T.; Hong, Wonpyo (Igen, Inc., USA). PCT Int. Appl. WO 9425573 A1 19941110, 98 pp. DESIGNATED STATES: W: AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, HU, JP, KG, KP, KR, KZ, LK, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ, VN; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1994-US4437 19940422. PRIORITY: US 1993-52490 19930423.

AB Described and claimed are compds. R1YNHCHR2X (I; Y = a polypeptide; R1 is bonded to the N-terminus of Y and is H or a branched, linear, substituted or unsubstituted C1-21-alkyl, -alkene, or -alkyne group; R2 = side chain of naturally occurring amino acid; X =P(:O)(OH)ME, P(:O)(OH)OMe, COCF3) or R1Y[(CH2)nX]m (II; R1, Y, and X as in I; n=1,2; m = integer ≤ total number of Asn and Gln in Y and (CH2)nX replaces Asn and Gln sidechains of Y) or R1CONHCHR2X (III; R1, R2, X as in I). Such compds. are useful as haptens and immunogens for the elicitation of antibodies which catalytically enhance the rate of formation or hydrolysis of primary amide bonds. The catalytic antibodies prepared by this method can be used in therapy, e.g. for hydrolysis of calcitonin. I compds. were prepared and used for monoclonal antibody production The monoclonal antibodies were screened for amidase activity.

L15 ANSWER 35 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN
1994:649443 Document No. 121:249443 Characterization of salt-soluble forms of acetylcholinesterase from bovine brain. Liao, Jian; Boschetti, Nicola; Mortensen, Vibeke; Jensen, Soeren Peter; Koch, Claus; Noegaard-Pedersen, Bent; Brodbeck, Urs (Institute of Biochemistry and Molecular Biology, University of Bern, Bern, Switz.). Journal of Neurochemistry, 63(4), 1446-53 (English) 1994. CODEN: JONRA9. ISSN: 0022-3042.

AB The hydrophilic, salt-soluble (SS) form of acetylcholinesterase (AChE) from bovine brain caudate nucleus exists mainly as a tetramer sedimenting at 10.3S (.apprx.40%) and a monomer sedimenting at 3.4S (.apprx.60%). The enzyme is N-glycosylated and contains HNK-1 carbohydrates similar to thoses of detergent-soluble (DS) AChE. No O-linked carbohydrates could be detected. Amino acid sequencing showed that the N terminus of SS-AChE is identical to that of DS-AChE. In tetrameric SS-AChE, two pairs of disulfide-linked dimers are associated by hydrophobic forces located in the C terminus. Antibodies were raised against a peptide identical to the last 10 amino acid residues of bovine brain DS-AChE. The peptide included the sequence of residues 574-583 (H-Tyr-Ser-Lys-Gln-Asp-Arg-Cys-Ser- Asp-Leu-OH) of the enzyme. The antibodies cross-reacted with tetrameric, but not with monomeric, SS-AChE, showing that in the latter form, the C terminus is truncated. Limited proteolysis of tetrameric SS-AchE at the C terminus led to the formation of an enzymically active monomer, which did not react with anti-C-terminal antibody. Although the DS form of AChE contains a structural subunit that serves as membrane anchor, no anchor was detected in SS-AChE. Enzyme antigen immunoassays showed that SS-AChE reacted with all monoclonal antibodies directed against the catalytic subunit of DS-AChE, but not with monoclonal antibodies targeting the membrane-anchored subunits. Thus, SS-AChE utilizes the same alternative splicing pattern as DS-AChE, leading to tetrameric SS-AChE devoid of the membrane anchor. The active monomer of SS-AChE is most likely derived from tetrameric forms by limited postsynthetic proteolysis.

L15 ANSWER 36 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN
1994:52225 Document No. 120:52225 Antibodies against active-site peptides common to glucosyltransferases of mutans streptococci. Cope, Patricia A.; Mooser, Gregory (Sch. Dent., Univ. South. California, Los Angeles, CA, 90089-0641, USA). Infection and Immunity, 61(11), 4814-17 (English) 1993. CODEN: INFIBR. ISSN: 0019-9567.

AB Polyclonal antibodies were raised against peptides derived from an active-site sequence common to the family of mutans streptococcal glucosyltransferases (GTFs). The sequence contains an aspartic acid residue that functions in formation of the enzyme transition state in catalysis. Two GTFs were targeted with similar but not identical sequences in

this region: one that synthesizes an α-1,3-linked water-insol. glucan and a homologous GTF that synthesizes in α-1,6-linked water-soluble glucan. For each enzyme, an 8-mer and 22-mer peptide were prepared The two peptide lengths were chosen to increase the likelihood of the peptides folding in a conformation similar to that of the native enzyme. Each peptide immunogen produced high titers of antibody, in rabbits, and all antisera cross-reacted with all peptides, albeit to various degrees. Native enzyme showed weak interaction with antisera, which, on the basis of enzyme denaturation expts., likely reflects binding to a small but finite population of denatured enzyme in the sample. GTF was assayed for inhibition in the presence of protein A-purified IgG from each antiserum. Given the mass of the antibody and catalytic importance of the peptide, any enzyme-antibody complex formation would result in enzyme inhibition. No inhibition was observed, which demonstrates that either polyclonal antibodies raised against each of the four peptides cannot access this active-site region, or antibodies do not recognize the native enzyme conformation. The advantages and challenges of generating antibodies against enzyme active-site peptides are discussed in the context of the crystal structure of Aspergillus oryzae α-amylase, which has a homologous peptide segment which serves the same catalytic function.

L15 ANSWER 37 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN

1993:186844 Document No. 118:186844 An inhibitory monoclonal anti-protein antibody and an anti-peptide antibody share an epitope on rat cytochrome P-450 enzymes CYP1A1 and CYP1A2. Edwards, Robert J.; Murray, Bernard P.; Murray, Stephen; Singleton, Alison M.; Davies, Donald S.; Boobis, Alan R. (Dep. Clin. Pharmacol., R. Postgrad. Med. Sch., London, UK). Biochimica et Biophysica Acta, Protein Structure and Molecular Enzymology, 1161(1), 38-46 (English) 1993. CODEN: BBAEDZ. ISSN: 0167-4838. Publisher: Elsevier B.V..

AB A monoclonal antibody, 12/2/3/2, which was raised against purified rat CYP1A1 recognizes specifically rat and mouse CYP1A1 and CYP1A2, but not any cytochrome P 450 present in hepatic microsomal fractions from rabbit, guinea pig, hamster or human. By comparing the primary sequences of cytochromes P 450 to which 12/2/3/2 does and does not bind, 10 possible locations for its epitope were found. Of these, one was extremely hydrophilic and, hence, predicted to be the most antigenic in the native protein. An antibody was produced against the synthetic peptide corresponding to this region (Gly-Arg-Asp-Arg-Gln-Pro-Arg-Leu: residues 356-363 and 350-357 of rat CYP1A1 and CYP1A2, resp.). The antibody bound to rat, mouse and hamster CYP1A1 and to rat and mouse CYP1A2, but did not bind to any protein present in hepatic microsomal fractions from the rabbit, guinea pig or human. The binding of the anti-peptide antibody to CYP1A1 or CYP1A2 was partially antagonized by the monoclonal antibody. However, whereas the monoclonal antibody inhibited both CYP1A1- (aryl hydrocarbon hydroxylase) and CYP1A2-(high-affinity phenacetin O-deethylase) dependent monooxygenase activity, the anti-peptide antibody was without effect on these activities. Antigen denaturation by 8 M urea or 0.05% (weight/volume) SDS had no effect on binding of the anti-peptide antibody to cytochrome P 450, whilst binding of the monoclonal antibody was reduced by more than 1000-fold. The anti-peptide antibody partially antagonized the binding of 12/2/3/2 to urea-denatured but not native cytochrome P 450. These data suggest that whilst the complete binding site for the monoclonal antibody is discontinuous, sufficient of the epitope is linear, so that when the antigen is denatured the monoclonal antibody is still able to bind and this binding is antagonized by the anti-peptide antibody. However, inhibition of catalytic activity by the monoclonal antibody must require binding to discontinuous residues.

L15 ANSWER 38 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN

1993:119690 Document No. 118:119690 Antibody-catalyzed rearrangement of the peptide bond. Gibbs, Richard A.; Taylor, Scott; Benkovic, Stephen J. (Dep. Chem., Pennsylvania State Univ., University Park, PA, 16802, USA). Science (Washington, DC, United States), 258(5083), 803-5 (English) 1992. CODEN: SCIEAS. ISSN: 0036-8075.

AB The generation of antibodies for a bifunctional cyclic phosphinate transition-state analog provided agents capable of efficiently catalyzing both steps of the overall conversion of a substrate containing an Asn -Gly sequence through a succinimide intermediate to the products Asp-Gly and the rearranged isoaspartyl-Gly sequence. This reaction provides a potential means in addition to amide cleavage for the deactivation of protein or peptide biol. functions in vivo.

L15 ANSWER 39 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN
1993:55060 Document No. 118:55060 The generation of antibody combining sites containing catalytic residues. Shokat, Kevan M.; Schultz, Peter G. (Dep. Chem., Univ. California, Berkeley, CA, 94720, USA). Ciba Foundation Symposium, 159(Catal. Antibodies), 118-34 (English) 1991. CODEN: CIBSB4. ISSN: 0300-5208.

AB To expand the scope of antibody-catalyzed reactions to those involving rate-limiting proton abstraction, such as elimination, isomerization, and condensation reactions, a new strategy, hapten charge complementarity, was developed. A hapten containing a benzylammonium group was used to elicit a specific base, a carboxylate, in the combining site of an antibody that catalyzed a β-elimination reaction. This was the first example of the use of a hapten to elicit a specific catalytic residue in an antibody combining site. A variety of kinetic and chemical modification expts. strongly suggest that a specific Asp or Glu residue in the combining site is responsible for catalysis. Preliminary results indicate that in addition to charge-charge complementarity, the nucleophilic reactivity of amino acid residues (Ser, Thr, Lys, Asp, Glu, Cys) in antibodies can be used as a selection tool. Antibodies were raised against a reactive epoxide group to elicit an antibody containing a uniquely reactive carboxylate or thiol group. Antibodies which bind the epoxide do catalyze a β-elimination reaction, indicating the presence of a specific base in the combining site. Antibodies elicited to two closely related haptens do not catalyze the β-elimination reaction.

L15 ANSWER 40 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN
1992:192479 Document No. 116:192479 Metal-binding Ig variable domain proteins. Lerner, Richard A.; Roberts, Victoria N.; Getzoff, Elisabeth D.; Tainer, John A.; Benkovic, Stephen J. (Scripps Clinic and Research Foundation, USA). PCT Int. Appl. WO 9116912 A1 19911114, 72 pp. DESIGNATED STATES: W: AU, CA, FI, JP, NO; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1991-US3149 19910507. PRIORITY: US 1990-521258 19900508; US 1990-539980 19900618.

AB The title proteins can form a coordination complex with a metal cation. The protein contains (1) a sequence of amino acid residues that defines a variable domain of an Ig; and (2) 3 contact amino acid residues in the variable domain of 1 that define a metal-binding site. Identification of Ig variable domain sites for introducing a metal ligand, as well as catalytic antibody design, are discussed. Recombinant production of QM212 (a single-chain antigen-binding protein derived from a light chain portion of an antifluorescein monoclonal antibody) is described. QM212 simultaneously bound both Cu(II) and fluorescein.

L15 ANSWER 41 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN
1992:1784 Document No. 116:1784 Walk-through mutagenesis. Crea, Roberto (USA). PCT Int. Appl. WO 9115581 A1 19911017, 92 pp. DESIGNATED STATES: W: AT, AU, BB, BG, BR, CA, CH, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MC, MG, MW, NL, NO, PL, RO, SD, SE, SU, US; RW: AT, BE, BF, BJ, CF, CG, CH, CM, DE, DK, ES, FR, GA, GB, GR, IT, LU, ML, MR, NL, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1991-US2362 19910405. PRIORITY: US 1990-505314 19900405.

AB A method for oligonucleotide-directed site-specific mutagenesis of a defined region of a gene that results in a series of analogs with a specific amino acid substituting for any amino acid in the region (walk-through mutagenesis) is described. The method uses a set of oligonucleotides with an appropriate codon at one of the positions within the coding region. The use of the method to generate analogs of the proteinase of human immunodeficiency virus with altered substrate specificities was demonstrated.

L15 ANSWER 42 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN
1991:674600 Document No. 115:274600 Determination of the epitope for the inhibitory monoclonal antibody 5-B6 on the catalytic subunit of gastric magnesium-dependent hydrogen ion-transporting and potassium-stimulated ATPase. Van Uem, Tom J. F.; Swarts, Herman G. P.; De

Pont, Jan Joep H. H. M. (Dep. Biochem., Univ. Nijmegen, Nijmegen, 6500 HB, Neth.). Biochemical Journal, 280(1), 243-8 (English) 1991. CODEN: BIJOAK. ISSN: 0306-3275.

AB Monoclonal antibody 5-B6, directed against the α-subunit of pig gastric (H+, K+)-ATPase (Mg2+-dependent H+-transporting and K+-stimulated ATPase), was previously shown to be a potent inhibitor of the K+-ATPase activity, thereby binding to the cytoplasmic side of the α-subunit of the enzyme. In order to define the epitope for 5-B6 on pig gastric (H+, K+-)ATPase more precisely, the α-subunit of the enzyme was subjected to limited proteolysis followed by chemical cleavage. Restricted proteolysis with papain followed by sequence anal. yielded an immunoreactive fragment of 27 kDa beginning at Ser379. This fragment was water-soluble and possessed the fluorescein isothyocyanate-reaction site. Limited tryptic digestion in the presence of K+ gave rise to an immunoreactive 56-kDa fragment beginning at Ile456, thus restricting the location of the epitope from Ile456 to the C-terminal end of the 27-kDa fragment (around residue 620). Further degradation of the 27-kDa fragment by means of formic acid cleavage at Asp-Pro bonds resulted initially in the formation of 2 nonimmunoreactive fragments of 17 and 11 kDa, indicating that the epitope for 5-B6 has to be localized around the chemical cleavage sites Asp507 and/or Asp510. Comparison of the primary structure of the α-subunits of gastric (H+, K+)-ATPase and nonimmunoreactive rat kidney (Na+, K+)-ATPase showed almost no similarity for the sequence containing these formic acid-cleavage sites (Thr504-Leu-Glu- Asp-Pro-Arg-Asp-Pro-Arg512), whereas the adjacent sequences were nearly 100% identical. These findings strongly suggest that the epitope for 5-B6 includes (part of) this sequence.

L15 ANSWER 43 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN

1975:591270 Document No. 83:191270 Effects of specific antibodies on the catalytic activity of L-asparaginase from Serratia marcescens and Escherichia coli. Ferguson, Donald A., Jr.; Phillips, Arthur W.; Marucci, Alvin (Dep. Biol., Syracuse Univ., Syracuse, NY, USA). Journal of Bacteriology, 124(1), 424-34 (English) 1975. CODEN: JOBAAY. ISSN: 0021-9193.

AB Rabbit antiserums to purified L-asparaginase from S. marcescens and E. coli showed up to 60% inhibition of catalytic hydrolysis of L- asparagine when combined with homologous enzyme. This inhibition was dimished somewhat against the heterologous enzyme. Kinetic studies in the presence of these antiserums showed an increased KMapp for both homologous and heterologous enzymes using L-asparagine as substrate. In contrast, kinetic studies employing the poor substrate, L-glutamine, showed activation attributable to specific antibodies. This was seen in lower KMapp values and up to 2-fold increases in the Vmax over the normal rabbit serum controls. The high degree of cross-inhibition (.apprx.80%) and the low degree of cross-reactivity in the quant. precipitin test (.apprx.34%) suggested that these 2 enzymes possessed structural similarities located mainly in the regions of the catalytic sites.

L15 ANSWER 44 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN

1975:55864 Document No. 82:55864 Immunoenzymology of L-asparaginase from the BCG strain of Mycobacterium bovis. Soru, Eugenia; Zaharia, Odette (Dep. Enzymol., Dr. I. Cantacuzino Inst., Bucharest, Rom.). Immunochemistry, 11(12), 791-5 (English) 1974. CODEN: IMCHAZ. ISSN: 0019-2791.

AB The antigenicity of a purified preparation of BCG-L-asparaginase was confirmed by the precipitating antibodies in the serum of California rabbits injected with this enzyme. The effect of BCG-L-antibodies on the catalytic activity of this enzyme was examined Three types of responses were recorded using immune γ-globulin, the immune Fab fragment, and the immune H-chain: viz. inhibition, stimulation, or no effect. This comparatively rare aspect is discussed. The intensity of inhibition and of stimulation depends on the ratio between enzyme and antienzyme antibodies, as well as on the preincubation interval between enzyme and antibodies. Both effects inhibition and stimulation are abolished by the specific substrate (L-asparagine) of this enzyme, so suggesting that for both, specific antibodies are involved.

L15 ANSWER 45 OF 45 CAPLUS COPYRIGHT 2006 ACS on STN

1973:511665 Document No. 79:111665 Basis for loss of therapeutic effectiveness of L-asparaginase in sensitized mice. Baechtel, Samuel; Prager, Morton D. (Southwest Med. Sch., Univ. Texas, Dallas, TX, USA).

Cancer Research, 33(8), 1966-9 (English) 1973. CODEN: CNREA8. ISSN: 0008-5472.

AB Loss of antitumor activity of L-asparaginase [9015-68-3] in sensitized mice apparently results from reduction of catalytic activity by antibody and extremely rapid clearance from the circulation. Upon sensitization of C3H mice to Escherichia coli L-asparaginase, antibody was produced that was inhibitory to the catalytic activity of the enzyme. Kinetic studies with antiserum showed that the inhibitory effect of antibody was due to a 3.6-fold reduction of Vmax. The Km for L- asparagine was only negligibly effected. The time for one-half the dose to be cleared from the plasma of unsensitized mice was 7.5 hr, this rate decreased to 27 hr in mice bearing the 6C3HED-R lymphoma. In sensitized animals, the time for half-clearance was 0.5 hr. In sensitized tumor-bearing mice no L-asparaginase was detectable in the circulation from 2 min to 24 hr after administration.

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=> E MULKERRIN M/AU

=> S E3-D7
         10485 E3
          2311 D7
L16          0 E3-D7
                 (E3(W)D7)

=> S E3-E7
             1 "MULKERRIN M"/AU
             3 "MULKERRIN M G"/AU
             3 "MULKERRIN MICHAEL"/AU
            32 "MULKERRIN MICHAEL G"/AU
             3 "MULKERRIN MICHAEL GEORGE"/AU
L17         42 ("MULKERRIN M"/AU OR "MULKERRIN M G"/AU OR "MULKERRIN MICHAEL"/A
               U OR "MULKERRIN MICHAEL G"/AU OR "MULKERRIN MICHAEL GEORGE"/AU)

=> E ZHANG R/AU

=> E ZHANG RUO/AU
=> S E23
L18         20 "ZHANG RUOHENG"/AU

=> E ROSKOS L/AU
=> S E3-E7
             2 "ROSKOS L"/AU
             2 "ROSKOS L K"/AU
            12 "ROSKOS LORIN"/AU
            11 "ROSKOS LORIN K"/AU
             1 "ROSKOS LORIN KARSTEN"/AU
L19         28 ("ROSKOS L"/AU OR "ROSKOS L K"/AU OR "ROSKOS LORIN"/AU OR "ROSKO
               S LORIN K"/AU OR "ROSKOS LORIN KARSTEN"/AU)

=> E BLUMBERG P/AU

=> E BLUMBERGS P/AU
=> S E3-E6
            10 "BLUMBERGS P"/AU
            10 "BLUMBERGS P C"/AU
            54 "BLUMBERGS PETER"/AU
             9 "BLUMBERGS PETER C"/AU
L20         83 ("BLUMBERGS P"/AU OR "BLUMBERGS P C"/AU OR "BLUMBERGS PETER"/AU
               OR "BLUMBERGS PETER C"/AU)

=> E LONESCU D/AU

=> S EE
         15195 EE
           624 EES
L21      15732 EE
                 (EE OR EES)
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=> S E3
L22             1 "LONESCU DUMITRU"/AU

=> S L17,L18,L19,L20,L22
L23           170 (L17 OR L18 OR L19 OR L20 OR L22)

=> S L23 AND L4
L24             1 L23 AND L4

=> D CBIB ABS

L24  ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2006 ACS on STN
2005:346675   Document No. 142:392665  Preparation of amino acid derivatives as
      asparagine deaminase catalytic antibodies.
      Mulkerrin, Michael G.; Zhang, Ruoheng; Roskos,
      Lorin; Blumbergs, Peter; Lonescu, Dumitru (USA).
      U.S. Pat. Appl. Publ. US 2005084488 A1 20050421, 15 pp.  (English).
      CODEN: USXXCO.  APPLICATION: US 2004-821626 20040409.  PRIORITY: US
      2003-462550P 20030410.
AB    Transition state analogs are described which may be used to elicit antibodies that
      catalyze the conversion of asparagine to aspartic acid. Synthetic schemes are disclosed
      for making the transition state analogs which can than be attached to a carrier mol. to
      form an immunoconjugate for administration to an animal for the purpose of raising
      antibodies. Antibodies can in turn be used in pharmaceutical compns. which can be given
      to patients as part of a method of treating various conditions, particularly cancer.
      Examples describe the synthesis of 2-(acetylamino)-N-(1,4-dihydroxy-1-oxophospholan-3-
      yl)acetamide and N-glycyl-L-phosphonamidylalanine.


=> S L23 AND (L12,L13)
L25             6 L23 AND ((L12 OR L13))

=> S L25 NOT (L24,L9,L15)
L26             5 L25 NOT ((L24 OR L9 OR L15))

=> D 1-5 CBIB ABS

L26  ANSWER 1 OF 5  CAPLUS  COPYRIGHT 2006 ACS on STN
1996:730696   Document No. 126:75227  Solid-phase synthesis, metal binding and
      folding properties of caulimovirus-related zinc finger'.  Ji, Hong;
      Zhang, Ruoheng; Lai, Luhua; Shao, Meicheng (Dept. of Chemistry,
      Peking Univ., Beijing, Peop. Rep. China).  International Journal of
      Peptide & Protein Research, 48(5), 461-464 (English) 1996.  CODEN: IJPPC3.
      ISSN: 0367-8377.  Publisher: Munksgaard.
AB    A 17-residue peptide H-Cys-Arg-Cys-Trp-Ile-Cys-Asn -Ile-Glu-Gly-His-Tyr-Ala-Asn-Glu-
      Cys-Pro-OH, containing the caulimovirus-related zinc finger was prepared by solid-phase
      peptide synthesis.  Fluorescence measurements showed that the Trp quantum yield was
      Zn2+ dependent, allowing a 1:1 stoichiometry for the complex to be determined  The
      structure of the peptide was characterized using CD, which indicates that the peptide
      exhibits a random coiled conformation in the absence of zinc but appears to form an
      ordered structure in the presence of zinc.


L26  ANSWER 2 OF 5  CAPLUS  COPYRIGHT 2006 ACS on STN
1995:397536   Document No. 122:154951  Ligand Binding to the Tissue-Type
      Plasminogen Activator Kringle 2 Domain: Structural Characterization by
      1H-NMR.  Byeon, In-Ja L.; Kelley, Robert F.; Mulkerrin, Michael G.
      ; An, Seong Soo A.; Llinas, Miguel (Department of Chemistry, Carnegie
      Mellon University, Pittsburgh, PA, 15213, USA).  Biochemistry, 34(9),
      2739-50 (English) 1995.  CODEN: BICHAW.  ISSN: 0006-2960.  Publisher:
      American Chemical Society.
AB    Ligand binding to a recombinant human tissue-type plasminogen (tPA) kringle 2 domain
      has been characterized via 1H-NMR spectroscopy at 500 MHz.  Seven ω-amino acid ligands
      were investigated: L-Lys, 6-aminohexanoic acid (6AHA), 7-aminoheptanoic acid (7AHA), p-
      (aminomethyl)cyclohexanecarboxylic acid (AMCHA), p-(aminomethyl)benzoic acid (PAMBA),
      p-(aminoethyl)benzoic acid (PAEBA), and p- benzylaminesulfonic acid (BASA).  The
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interactions with two peptides containing a C-terminal lysyl residue, Tyr-Leu-Leu-Lys (YLLK) and Ala-Phe-Gln-Tyr-His-Ser-Lys (AFQYHSK), were also studied. The heptapeptide AFQYHSK is found in the plasminogen N-terminal activation peptide while the tetrapeptide YLLK corresponds the 119-122 segment of the fibrinogen Bβ-chain. Spectral comparison of ligand-free and ligand-containing kringle 2 samples leads to the conclusion that all the small ligands as well as the peptides' C-terminal lysyl residues interact with a common binding site in kringle 2. Two-dimensional spectra show that besides the Tyr36, Trp62, His64, Trp72, and Tyr74 aromatic rings, the Val35 and Asp55 aliphatic side chains also participate in ligand binding. Contact points with the ligands 6AHA and BASA were unambiguously identified from kringle 2-ligand nuclear Overhauser effects (NOEs). Overall, the ligand-induced chemical shifts and the intermol. NOEs correlate remarkably well. Association constant (Ka) values for the kringle 2-ligand interactions were determined Among the investigated ligands, BASA perturbs the kringle 2 spectrum the most and exhibits the highest affinity for kringle 2 (Ka .apprx. 233 mM-1). Of the two other aromatic ligands, PAEBA binds to kringle 2 less firmly (Ka = .apprx.12 mM-1) than does the one-methylene group shorter analog PAMBA (Ka .apprx. 31 mM-1). By comparison, relative to 6AHA (Ka .apprx. 22 mM-1), the longer chain linear aliphatic ligand 7AHA interacts with kringle 2 with significantly higher affinity (Ka .apprx. 149 mM-1). By reference to the NMR-derived binding site structure, it is suggested that the higher affinity toward 7AHA may stem from (a) a relatively more favored ionic pairing between its carboxylate group and the Lys34 + Arg69 side-chain cationic centers and (b) an enhanced interaction between the ligand hydrocarbon moiety and the kringle hydrophobic pocket, in particular with the Leu70 side chain. The latter is consistent with the relatively good affinity of kringle 2 for the cyclic hydrocarbon ligand AMCHA (Ka .apprx. 69 mM-1). When compared against L-Lys (Ka .apprx. 18 mM-1), the higher affinity exhibited by YLLK and AFQYHSK (Ka .apprx. 38 mM-1) indicates that the attached polypeptide chain segments contribute pos. to their binding to kringle 2. Overall, the NMR ligand-binding data are in harmony with the binding site structure, solvent accessibility, and pH sensitivity of individual residues and confirm, as found for other kringles, that the ligand complexation event is not accompanied by any significant conformational change of the kringle fold.

L26 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2006 ACS on STN

1994:646579 Document No. 121:246579 Conformational Changes in the Reversed Phase Liquid Chromatography of Recombinant Human Growth Hormone as a Function of Organic Solvent: The Molten Globule State. Wicar, S.; Mulkerrin, M. G.; Bathory, G.; Khundkar, L. H.; Karger, B. L. (Barnett Institute, Northeastern University, Boston, MA, 02115, USA). Analytical Chemistry, 66(22), 3908-15 (English) 1994. CODEN: ANCHAM. ISSN: 0003-2700.

AB As a continuation of a previous paper on the retention behavior of recombinant human growth hormone (rhGH) in reversed phase chromatog. at pH 6.5 (P. Oroszlan, P., et al. Anal. Chemical 1992, 64, 1623-1631) the effect of 1-propanol (1-PrOH) and acetonitrile on the conformation of rhGH at this pH has been investigated by CD, second-derivative UV spectroscopy, fluorescence anisotropy, fluorescence quenching, and fluorescence lifetime measurements. Addition of 1-PrOH up to a concentration of 10% (volume/volume) does not cause any significant changes in protein structure. However, above this concentration, a transition from the native to a new state is observed; the transition is completed above 30% (volume/volume) of 1-PrOH, the composition for completion being dependent on temperature This change in structure correlates with retention changes observed in reversed phase chromatog. The new rhGH conformation retains much of the α-helicity and possesses a slightly expanded hydrodynamic radius relative to native rhGH. Second-derivative UV spectroscopy suggests that the hydrogen bond between Trp 86 and Asp 169, spanning two α-helixes, remains intact. The near-UV CD intensity changes from pos. to neg. in the Trp region of the spectrum, signaling an alteration in the Trp environment. In addition, fluorescence quenching measurements with trichloroethanol reveal greater accessibility to solvent of the Trp residue after the conformational transition has occurred. From the results, it is concluded that a molten globule state (compact state retaining much of the secondary structure of the native state but with a disrupted tertiary structure) is produced with the addition of >30% (volume/volume) 1-PrOH. In the case of CH3CN, no significant conformational changes are observed up to 40% (volume/volume) and at temps. up to 40°. This study provides insight into the mechanism of reversed phase chromatog. retention of rhGH and the general role of organic solvents on protein structure.

L26 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2006 ACS on STN

1993:603803 Document No. 119:203803 Preparation of partially protected peptide thioesters containing a cysteine residue and their segment condensation. Kwon, Yeondae; Zhang, Ruoheng; Bemquerer, Marcelo P.; Tominaga, Mineko; Hojo, Hironobu; Aimoto, Saburo (Inst. Protein Res., Osaka Univ., Suita, 565, Japan). Chemistry Letters (5), 881-4 (English) 1993. CODEN: CMLTAG. ISSN: 0366-7022. OTHER SOURCES: CASREACT 119:203803.

GI For diagram(s), see printed CA Issue.

AB Methods for the preparation of partially-protected cysteine-containing peptide segments were developed. The peptide thioester, obtained via a solid-phase method of Boc chemical, was used for segment condensation with an amino component peptide in the presence of silver ions and N-hydroxysuccinimide (HONSu) to give a desired product in good yield. Thus, Boc-Ser-Leu-Arg-Arg-Ser-Ser-Cys(MeBzl)-Phe-Gly-SCMe2CH2CO-Nle-NH2 (I; MeBzl = 4-methylbenzyl) was coupled with H-Gly-Arg-Met-Asp -Arg-Ile-Gly-Ala-Gln-Ser-Gly-Leu-Gly-Cys(MeBzl)-Asn -Ser-Phe-Arg-Tyr-OH in the presence of AgNO3, HONSu and N-methylmorpholine in DMSO to give peptide II. II was converted into hANP(1-28) III (hANP = human atrial natriuretic factor). I was obtained via the solid-phase method.

L26 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2006 ACS on STN

1993:443997 Document No. 119:43997 Synthesis and kinetics of chromogenic substrates for chymotrypsin. Zhang, Ruoheng; Ge, Xue; Xu, Xiaojie; Tang, Youqi (Dep. Chem., Peking Univ., Beijing, 100871, Peop. Rep. China). Gaodeng Xuexiao Huaxue Xuebao, 14(1), 144-6 (Chinese) 1993. CODEN: KTHPDM. ISSN: 0251-0790.

AB Five chromogenic substrates for chymotrypsin, P3-P2-P1-p-NA (P1, P2, P3 = Phe, Leu, Ala, Pro, Asn, p-NA = p-nitroanilide), have been synthesized. The influence of amino acid on the specificity was observed by kinetic anal. of the hydrolysis of the peptide by bovine chymotrypsin. Though most of the substrates are suitable for reaction with chymotrypsin, Ala-Ala-Phe-p-NA is the best.

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FILE 'REGISTRY' ENTERED AT 09:30:30 ON 24 JUL 2006

=> S ASPARAGINE DEAMINASE/CN
L1            0 ASPARAGINE DEAMINASE/CN

FILE 'CAPLUS' ENTERED AT 09:31:07 ON 24 JUL 2006

=> ACTIVATE ABZYME/Q
L2              QUE  ABB=ON  PLU=ON  ((CATALYSIS OR CATALYZES OR CATALYTIC OR C
                ATALYZED)(5A)ANTIBOD?) OR ABZYME

=> S L2
         183635 CATALYSIS
            424 CATALYSES
         183880 CATALYSIS
                  (CATALYSIS OR CATALYSES)
          36232 CATALYZES
         409364 CATALYTIC
             26 CATALYTICS
         409373 CATALYTIC
                  (CATALYTIC OR CATALYTICS)
         237243 CATALYZED
              1 CATALYZEDS
         237243 CATALYZED
                  (CATALYZED OR CATALYZEDS)
         466583 ANTIBOD?
           2370 (CATALYSIS OR CATALYZES OR CATALYTIC OR CATALYZED)(5A)ANTIBOD?
            262 ABZYME
            171 ABZYMES
            317 ABZYME
                  (ABZYME OR ABZYMES)
L3         2402 ((CATALYSIS OR CATALYZES OR CATALYTIC OR CATALYZED)(5A)ANTIBOD?)
                 OR ABZYME

=> S APARAGINE DEAMINASE
              7 APARAGINE
          13572 DEAMINASE
           1100 DEAMINASES
          13750 DEAMINASE
                  (DEAMINASE OR DEAMINASES)
L4            0 APARAGINE DEAMINASE
                  (APARAGINE(W)DEAMINASE)

=> S DEAMINASE
          13572 DEAMINASE
           1100 DEAMINASES
L5         13750 DEAMINASE
                  (DEAMINASE OR DEAMINASES)

=> S L5 AND L3
L6            4 L5 AND L3

=> D 1-4 CBIB ABS

L6  ANSWER 1 OF 4  CAPLUS  COPYRIGHT 2006 ACS on STN
2005:346675   Document No. 142:392665  Preparation of amino acid derivatives as
     asparagine deaminase catalytic antibodies.
     Mulkerrin, Michael G.; Zhang, Ruoheng; Roskos, Lorin; Blumbergs, Peter;
     Lonescu, Dumitru (USA).  U.S. Pat. Appl. Publ. US 2005084488 A1 20050421,
     15 pp.  (English).  CODEN: USXXCO.  APPLICATION: US 2004-821626 20040409.
     PRIORITY: US 2003-462550P 20030410.
AB   Transition state analogs are described which may be used to elicit antibodies that
     catalyze the conversion of asparagine to aspartic acid. Synthetic schemes are disclosed
     for making the transition state analogs which can than be attached to a carrier mol. to
     form an immunoconjugate for administration to an animal for the purpose of raising
     antibodies. Antibodies can in turn be used in pharmaceutical compns. which can be given
     to patients as part of a method of treating various conditions, particularly cancer.
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Examples describe the synthesis of 2-(acetylamino)-N-(1,4-dihydroxy-1-oxophospholan-3-yl)acetamide and N-glycyl-L-phosphonamidylalanine.

L6 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN

2004:824012 Document No. 141:308660 Fumonisin detoxification enzyme gene isolated from environmental microorganisms, compositions and methods for making fumonisin-resistant transgenic plants, and detoxification for grains and foods and feeds. Zhao, Lishan; Weiner, David Paul; Hickle, Leslie (Diversa Corporation, USA). PCT Int. Appl. WO 2004085624 A2 20041007, 254 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2004-US9054 20040324. PRIORITY: US 2003-457824P 20030324; US 2003-475042P 20030530; US 2003-480071P 20030619.

AB In one aspect, the invention provides methods of enzymic detoxification of aminated toxins, e.g., mycotoxins, such as fumonisin. The invention provides methods to enzymically detoxify plants, foods or feeds or any contaminated product or surface, including detoxification of mycotoxins, such as fumonisin, e.g., fumonisin B1 and fumonisin B2. The invention provides methods to prevent the contamination of plants, foods or feeds or any contaminated product or surface by application or a polypeptide having a deaminase activity. In one aspect, the invention relates to protein and cDNA sequences of 44 polypeptides having an aminotransferase, an aminomutase and/or a deaminase activity isolated from environmental microorganisms.

L6 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN

2003:503635 Document No. 139:160698 Processive AID-catalyzed cytosine deamination on single-stranded DNA simulates somatic hypermutation. Pham, Phuong; Bransteitter, Ronda; Petruska, John; Goodman, Myron F. (University of Southern California, Hedco Molecular Biology Laboratories, Departments of Biological Sciences and Chemistry, University Park, Los Angeles, CA, 90089-1340, USA). Nature (London, United Kingdom), 424(6944), 103-107 (English) 2003. CODEN: NATUAS. ISSN: 0028-0836. Publisher: Nature Publishing Group.

AB Activation-induced cytidine deaminase (AID) is a protein required for B cells to undergo class switch recombination and somatic hypermutation (SHM)-two processes essential for producing high-affinity antibodies. Purified AID catalyzes the deamination of C to U on single-stranded (ss)DNA. Here, we show in vitro that AID-catalyzed C deaminations occur preferentially on 5' WRC sequences in accord with SHM spectra observed in vivo. Although about 98% of DNA clones suffer no mutations, most of the remaining mutated clones have 10-70 C to T transitions per clone. Therefore, AID carries out multiple C deaminations on individual DNA strands, rather than jumping from one strand to another. The avid binding of AID to ssDNA could result from its large net pos. charge (+11) at pH 7.0, owing to a basic amino-terminal domain enriched in arginine and lysine. Furthermore, AID exhibits a 15-fold preference for C deamination on the non-transcribed DNA strand exposed by RNA polymerase than the transcribed strand protected as a RNA-DNA hybrid. These deamination results on ssDNA bear relevance to three characteristic features of SHM: preferential mutation at C sites within WRC hotspot sequences, the broad clonal mutagenic heterogeneity of antibody variable regions targeted for mutation, and the requirement for active transcription to obtain mutagenesis.

L6 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN

1995:412729 Document No. 122:151369 Modified glycosidation of fusion proteins of anti-tumor antibodies and prodrug activating enzymes and the use of the proteins in the targetted treatment of tumors. Bosslet, Klaus; Czech, Joerg; Hoffmann, Dieter (Behringwerke AG, Germany). Eur. Pat. Appl. EP 623352 A2 19941109, 28 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE. (English). CODEN: EPXXDW. APPLICATION: EP 1994-106394 19940425. PRIORITY: DE 1993-4314556

19930504.

AB Bifunctional antibody-enzyme conjugates with a modified glycosidation patterns are described for use in the treatment of tumors. The antibody component of the conjugate specifically binds a tumor-specific antigen and the enzyme moiety activates a prodrug. The carbohydrate component includes at least one exposed carbohydrate residue selected from the group: mannose, galactose, N-acetylglucosamine, N-acetyllactose, glucose and fucose and the exposed group is generated by enzymic removal of terminal sialic acid or mannose groups with optional enzymic addition of the new terminal sugar. Glycosidation contributes to increased relative concentration of the glycoproteins at the site of the tumor, and speeds clearance of the protein from the general circulation and non-tumor sites. The proteins are manufactured with a mammalian glycosidation pattern by expression of the cloned gene in a transgenic animal cell line or animal. Clearance studies carried out in CD-1 nude mice on glycosidated and non-glycosidated fusion proteins of a human β-glucuronidase and a human antibody to a tumor antigen are presented.

```
=> S ASPARAGINE DEAMINASE
         30531 ASPARAGINE
           311 ASPARAGINES
         30649 ASPARAGINE
                 (ASPARAGINE OR ASPARAGINES)
         13572 DEAMINASE
          1100 DEAMINASES
         13750 DEAMINASE
                 (DEAMINASE OR DEAMINASES)
L7           6 ASPARAGINE DEAMINASE
                 (ASPARAGINE(W)DEAMINASE)

=> S L7 AND L3
L8           1 L7 AND L3

=> S L8 NOT L6
L9           0 L8 NOT L6
```

	L #	Hits	Search Text	DBs
1	L1	3100	((catalysis or catalyzes or catalytic or catalyzed) near5 antibod$) or abzyme$	US-PGPUB; USPAT
2	L2	63459	ASPARAGINE OR ASN	US-PGPUB; USPAT
3	L3	60229	(ASPARATIC ACID) OR ASP	US-PGPUB; USPAT
4	L4	1502	L1 AND (L2 OR L3)	US-PGPUB; USPAT
5	L5	35	L1 SAME (L2 OR L3)	US-PGPUB; USPAT
6	L6	1	ASPARAGINE ADJ DEAMINASE	US-PGPUB; USPAT
7	L7	0	ASN ADJ DEAMINASE	US-PGPUB; USPAT